ClinicalTrials.gov ID: NCT01453348

Study Identification

Unique Protocol ID:	V59_53
Brief Title:	Study to Evaluate the Safety and Immunogenicity of Combined Hepatitis A/B Vaccine With MenACWY-CRM Conjugate Vaccine
Official Title:	A Phase 3b, Randomized, Open-Label Study to Evaluate the Safety and Immunogenicity of Combined Hepatitis A/B Vaccine When Administered Concomitantly With Novartis Meningococcal ACWY Conjugate Vaccine in Healthy Adults
Secondary IDs:	2011-001333-17 [EudraCT Number]

Study Status

Record Verification:	November 2015
Overall Status:	Completed
Study Start:	October 2011
Primary Completion:	January 2012 [Actual]
Study Completion:	January 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Novartis
Responsible Party:	Sponsor
Collaborators:	Novartis Vaccines

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: Project number: 258-11 Board Name: Ethic Comittee LMU München Board Affiliation: Board of Physicans, München Phone: +49 (0) 89 5160-5191 Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Germany: Federal Institute for Drugs and Medical Devices

Study Description

Brief Summary:	This study compares the safety and immunogenicity profile of combined hepatitis A/B vaccine given alone or concomitantly with MenACWY-CRM to healthy adults.
Detailed Description:	

Conditions

Conditions:	Meningococcal Disease Meningococcal Meningitis Hepatitis A Hepatitis B
Keywords:	meningococcal conjugate vaccine adults

Study Design

Study Type:	Interventional
Primary Purpose:	Prevention
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	3

Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	252 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Group 1 This group will receive Inactivated hepatitis A and recombinant hepatitis B or 'Combined inactivated hepatitis A & recombinant hepatitis B vaccine' alone on the different visits.	Biological/Vaccine: Combined inactivated hepatitis A & recombinant hepatitis B Combined inactivated hepatitis A and recombinant hepatitis B vaccine will be administered by IM on days 1, 8 & 29 for subjects unprimed with hepatitis A and B; and a single booster injection on day 1 for primed subjects. Biological/Vaccine: Recombinant hepatitis B vaccine Recombinant hepatitis B vaccine will be administered intramuscularly on days 8 and 29 Biological/Vaccine: Inactivated hepatitis A vaccine Inactivated hepatitis A will be administered intramuscularly on days 8 and 29.
Active Comparator: Group 2 This group will receive Inactivated hepatitis A vaccine and recombinant hepatitis B Vaccine or 'Combined inactivated hepatitis A & recombinant hepatitis B vaccine' concomitantly with MenACWY-CRM.	Biological/Vaccine: MenACWY-CRM Novartis meningococcal ACWY conjugate vaccine will be administered intramuscularly (IM) on day 1. Biological/Vaccine: Combined inactivated hepatitis A & recombinant hepatitis B Combined inactivated hepatitis A and recombinant hepatitis B vaccine will be administered by IM on days 1, 8 & 29 for subjects unprimed with hepatitis A and B; and a single booster injection on day 1 for primed subjects. Biological/Vaccine: Recombinant hepatitis B vaccine Recombinant hepatitis B vaccine will be administered intramuscularly on days 8 and 29 Biological/Vaccine: Inactivated hepatitis A vaccine Inactivated hepatitis A will be administered intramuscularly on days 8 and 29.
Active Comparator: Group 3 This group will receive only MenACWY-CRM.	Biological/Vaccine: MenACWY-CRM Novartis meningococcal ACWY conjugate vaccine will be administered intramuscularly (IM) on day 1.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 64 Years

Gender: Both

Accepts Healthy Volunteers?: Yes

Criteria: Inclusion Criteria:

Individuals eligible for enrollment in this study were female and male subjects who had shown to be healthy and who were:

1. Between 18 and 64 years of age inclusive and who had given their written informed consent;
2. Available for all visits and telephone calls scheduled for the study;
3. In good health as determined by medical history, physical examination and clinical judgment of the investigator;
4. For female subjects, had a negative urine pregnancy test.

Exclusion Criteria:

Individuals not eligible to be enrolled in the study were those:

1. Who were breastfeeding.
2. Who had a previous personal history of Neisseria meningitidis, hepatitis A or hepatitis B infection.
3. Who received previous immunization with any meningococcal vaccine.
4. Who received previous hepatitis A and/or B vaccination, determined by history (interview of the subject) and/or by review of his or her vaccination card, if less than 5 years have elapsed since vaccination.
5. Who received investigational agents or vaccines within 30 days prior to enrollment or who expected to receive an investigational agent or vaccine prior to completion of the study.
6. Who received live licensed vaccines within 30 days and inactive vaccine within 15 days prior to enrollment or for whom receipt of a licensed vaccine was anticipated during the study period (Exception: Influenza vaccine might have been administered up to 15 days prior to each study immunization and no less than 15 days after each study immunization).
7. Who experienced, within the 7 days prior to enrollment, significant acute infection (for example requiring systemic antibiotic treatment or antiviral therapy) or had experienced fever (defined as body temperature ≥ 38°C) within 3 days prior to enrollment.
8. Who had any serious acute, chronic or progressive disease such as:
    - History of cancer
    - Complicated diabetes mellitus
    - Advanced arteriosclerotic disease
    - Autoimmune disease
    - HIV infection or AIDS
    - Blood dyscrasias

- Congestive heart failure
- Renal failure
- Severe malnutrition (Note: Subjects with mild asthma were eligible for enrollment. Subjects with moderate or severe asthma requiring routine use of inhaled or systemic corticosteroids were not eligible for enrollment).

9. Who had epilepsy, any progressive neurological disease or history of Guillain-Barre syndrome.
10. Who had a history of anaphylaxis, serious vaccine reactions, or allergy to any vaccine component, including but not limited to latex allergy and antibiotic allergy.
11. Who had a known or suspected impairment/alteration of immune function, either congenital or acquired or resulting from (for example):

    - Receipt of immunosuppressive therapy within 30 days prior to enrollment (systemic corticosteroids administered for more than 5 days, or in a daily dose > 1 mg/kg/day prednisone or equivalent during any of 30 days prior to enrollment, or cancer chemotherapy);
    - Receipt of immunostimulants;
    - Receipt of parenteral immunoglobulin preparation, blood products, and/or plasma derivatives within 90 days prior to enrollment and for the full length of the study.

12. Who were known to have a bleeding diathesis, or any condition that might have been associated with a prolonged bleeding time.
13. Who had any condition that, in the opinion of the investigator, might have interfered with the evaluation of the study objectives.
14. Who were part of the study personnel or close family members of those conducting this study.

Contacts/Locations

Study Officials: Novartis Vaccines
Study Chair
Novartis Vaccines and Diagnostics

Locations: Germany
01, Novartis Investigational Site
München, Germany, 80802

02, Novartis Investigational Site
Hamburg, Germany, 20359

03, Novartis Investigational Site
Berlin, Germany, 10117

04, Novartis Investigational Site
Rostock, Germany, 18057

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Subjects were enrolled at four centers in Germany.
Pre-Assignment Details	All enrolled subjects were included in the trial.

Reporting Groups

	Description
HepA/B	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine.
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who received one dose of MenACWY-CRM conjugate vaccine.

Overall Study

	HepA/B	HepA/B+MenACWY-CRM	MenACWY-CRM
Started	84	84	84
Completed	83	83	83
Not Completed	1	1	1
Death	0	0	1
Withdrawal by Subject	0	1	0
Protocol Violation	1	0	0

Baseline Characteristics

Reporting Groups

	Description
HepA/B	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine.
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who received one dose of MenACWY-CRM conjugate vaccine.

Baseline Measures

	HepA/B	HepA/B+MenACWY-CRM	MenACWY-CRM	Total
Number of Participants	84	84	84	252

	HepA/B	HepA/B+MenACWY-CRM	MenACWY-CRM	Total
Age, Continuous [units: years] Mean (Standard Deviation)	39.0 (12.3)	39.9 (12.6)	39.7 (11.0)	39.5 (11.9)
Gender, Male/Female [units: participants]				
Female	45	40	50	135
Male	39	44	34	117

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Geometric Mean antiHAV and antiHBV Concentrations (GMCs), 28 Days After Primary and Booster Vaccination
Measure Description	Assessment was made to demonstrate the non-inferiority of hepatitis A/B vaccine with MenACWY-CRM as compared to hepatitis A/B vaccine without MenACWY-CRM, as measured by geometric mean concentrations on day 57 in previously unvaccinated subjects or on day 29 after a booster dose in previously vaccinated subjects.
Time Frame	Day 57 (previously unprimed subjects) day 29 (previously primed subjects) postvaccination.
Safety Issue?	No

Analysis Population Description

Analysis was done on Per Protocol (PP) population who provided evaluable serum samples and whose assay results were available at the relevant time points, and had no major protocol deviations

Reporting Groups

	Description
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine ; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.

	Description
HepA/B	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine.

Measured Values

	HepA/B+MenACWY-CRM	HepA/B
Number of Participants Analyzed	78	78
Geometric Mean antiHAV and antiHBV Concentrations (GMCs), 28 Days After Primary and Booster Vaccination [units: Concentrations (mIU/mL)] Geometric Mean (95% Confidence Interval)		
Prevaccination AntiHAV	48 (27 to 85)	30 (17 to 54)
28 days after primary or booster AntiHAV	786 (591 to 1046)	884 (664 to 1176)
Prevaccination AntiHBV (N=78, 76)	22 (12 to 39)	31 (17 to 57)
28 days after primary or booster AntiHBV (N=78,76)	844 (513 to 1387)	711 (429 to 1179)

Statistical Analysis 1 for Geometric Mean antiHAV and antiHBV Concentrations (GMCs), 28 Days After Primary and Booster Vaccination

Statistical Analysis Overview	Comparison Groups	HepA/B+MenACWY-CRM, HepA/B
	Comments	The primary criterion for immunogenicity was that the lower-limit of the two-sided 95% Confidence Interval (CI) on the ratio of Enzyme-linked Immunosorbent Assay (ELISA) GMCs (Hep A/B + MenACWY-CRM to Hep A/B) is below or equal to 0.5.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	(GMC anti-HAV + MenACWY-CRM / GMC anti-HAV)

Statistical Test of Hypothesis	P-Value	
	Comments	The testing was done by assessing the confidence interval of the ratio
	Method	ANCOVA

	Comments	The Analysis of variance (ANCOVA) model included vaccine group and center as factors, age as covariate and was adjusted for baseline.

Method of Estimation	Estimation Parameter	Other [Ratio of GMC]
	Estimated Value	0.89
	Confidence Interval	(2-Sided) 95% 0.6 to 1.32
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Geometric Mean antiHAV and antiHBV Concentrations (GMCs), 28 Days After Primary and Booster Vaccination

Statistical Analysis Overview	Comparison Groups	HepA/B+MenACWY-CRM, HepA/B
	Comments	The primary criterion for immunogenicity was that the the lower-limit of the two-sided 95% CI on the ratio of ELISA GMCs (Hep A/B + MenACWY-CRM to Hep A/B) is below or equal to 0.5.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	(GMC anti-HBsAg + MenACWY-CRM / GMC anti-HBsAg)

Statistical Test of Hypothesis	P-Value	
	Comments	The testing was done by assessing the confidence interval of the ratio
	Method	ANCOVA
	Comments	The ANCOVA model included vaccines group and center as factors, age as covariate and was adjusted for baseline.

Method of Estimation	Estimation Parameter	Other [Ratio of GMC]
	Estimated Value	1.19
	Confidence Interval	(2-Sided) 95% 0.59 to 2.37
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percentages of Subjects With antiHAV and antiHBsAg Antibodies Concentrations Above Seroprotection Level 28 Days After Primary or Booster Vaccination
Measure Description	Immunogenicity was assessed as the percentages of subjects with anti-HAV concentration ≥20 mIU/mL and anti-HBsAg antibody concentration ≥10 mIU/mL, 28 days after primary or booster vaccination.

Time Frame	28 days post primary or booster vaccination.
Safety Issue?	No

Analysis Population Description

Analysis was done on modified intention-to-treat (MITT) population- subjects who provided evaluable serum samples whose assay results are available for at least one antigen on visit day 1 and a post baseline visit.

Reporting Groups

	Description
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine ; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
HepA/B	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine.

Measured Values

	HepA/B+MenACWY-CRM	HepA/B
Number of Participants Analyzed	83	82
Percentages of Subjects With antiHAV and antiHBsAg Antibodies Concentrations Above Seroprotection Level 28 Days After Primary or Booster Vaccination [units: percentage of subjects] Number (95% Confidence Interval)		
AntiHAV antibody concentration ≥20mIU/mL (Day 1)	42 (31 to 54)	33 (23 to 44)
28 days after primary/booster AntiHAV	96 (90 to 99)	99 (93 to 100)

	HepA/B+MenACWY-CRM	HepA/B
AntiHBsAg antibody concentration ≥10mIU/mL (Day 1)	47 (36 to 58)	44 (33 to 55)
28 days after primary/booster AntiHBV	75 (64 to 84)	80 (70 to 88)

3. Secondary Outcome Measure:

Measure Title	Percentages of Subjects With Seroresponse Against N Meningitidis A, C, W and Y Serogroups at Day 29
Measure Description	Immunogenicity was assessed as the seroresponse rates for meningococcal serogroups A, C, W and Y elicited by MenACWY-CRM on day 29 when given concomitantly with combined hepatitis A/B vaccine or given alone. For a subject with a baseline hSBA titer < 1:4, seroresponse is defined as a postvaccination hSBA titer ≥1:8; for a subject with a baseline hSBA titer ≥ 1:4, seroresponse is defined as a postvaccination hSBA titer of at least 4 times the baseline.
Time Frame	28 days postvaccination (day 29).
Safety Issue?	No

Analysis Population Description

Analysis was done on modified intention-to-treat (MITT) population- subjects who provided evaluable serum samples whose assay results are available for at least one antigen on visit day 1 and a post baseline visit.

Reporting Groups

	Description
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine ; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who received one dose of MenACWY-CRM conjugate vaccine.

Measured Values

	HepA/B+MenACWY-CRM	MenACWY-CRM
Number of Participants Analyzed	83	83

	HepA/B+MenACWY-CRM	MenACWY-CRM
Percentages of Subjects With Seroresponse Against N Meningitidis A, C, W and Y Serogroups at Day 29 [units: percentage of subjects] Number (95% Confidence Interval)		
MenA-hSBA Overall Seroresponse (N=83, 82)	71 (60 to 81)	65 (53 to 75)
MenC-hSBA Overall Seroresponse	66 (55 to 76)	59 (48 to 70)
MenW-hSBA Overall Seroresponse (N=83, 82)	40 (29 to 51)	34 (24 to 45)
MenY-hSBA Overall Seroresponse	70 (59 to 79)	64 (53 to 74)

4. Secondary Outcome Measure:

Measure Title	hSBA GMTs Assay Titers Against N Meningitidis A, C, W and Y Serogroups at Day 29
Measure Description	Immunogenicity was assessed in terms of geometric mean titers (GMTs) of antibodies to meningococcal serogroups A, C, W and Y on day 29 when given concomitantly with combined hepatitis A/B vaccine or given alone.
Time Frame	28 days post vaccination (day 29).
Safety Issue?	No

Analysis Population Description

Analysis was done on modified intention-to-treat (MITT) population- subjects who provided evaluable serum samples whose assay results are available for at least one antigen on visit day 1 and a post baseline visit.

Reporting Groups

	Description
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine ; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who received one dose of MenACWY-CRM conjugate vaccine.

Measured Values

	HepA/B+MenACWY-CRM	MenACWY-CRM
Number of Participants Analyzed	84	84
hSBA GMTs Assay Titers Against N Meningitidis A, C, W and Y Serogroups at Day 29 [units: Titers] Geometric Mean (95% Confidence Interval)		
MenA-Human Complement-SBA - Day 1	2.68 (2.27 to 3.17)	2.71 (2.29 to 3.2)
Day 29 (N=83, 82)	43 (27 to 67)	36 (23 to 58)
MenC-Human Complement-SBA - Day 1	7.39 (5.49 to 9.94)	6.35 (4.71 to 8.57)
Day 29 (N=83, 83)	75 (50 to 112)	56 (37 to 83)
MenW-hSBA - Day 1 (N=84,83)	30 (21 to 42)	31 (22 to 45)
Day 29 (N=83, 83)	110 (84 to 145)	109 (82 to 144)
MenY-hSBA - Day 1	6.63 (5.06 to 8.68)	5.56 (4.23 to 7.3)
Day 29 (N=83, 83)	78 (55 to 111)	62 (44 to 89)

5. Secondary Outcome Measure:

Measure Title	Percentages of Subjects With Unsolicited Adverse Events (AEs)
Measure Description	Safety was assessed in terms of percentage of all spontaneously reported AEs collected from the time the subject signed the informed consent form (day 1), until the subject stopped study participation (day 57).
Time Frame	Day 1 to day 57.
Safety Issue?	Yes

Analysis Population Description

Analysis was done on safety set- subjects who provided any post-baseline safety data.

Reporting Groups

	Description
HepA/B	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine.
HepA/B+MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
MenACWY-CRM	Subjects ≥ 18 to ≤ 64 years of age who received one dose of MenACWY-CRM conjugate vaccine.

Measured Values

	HepA/B	HepA/B+MenACWY-CRM	MenACWY-CRM
Number of Participants Analyzed	84	85	83
Percentages of Subjects With Unsolicited Adverse Events (AEs) [units: percentage of subjects]			
Any AE	43	39	36
Atleast possibly related AE	23	27	17
Any SAE	1	0	1
AE leading to withdrawal	0	1	1
Death	0	0	1

Reported Adverse Events

Time Frame	Day 1 to day 57.
Additional Description	Safety was assessed in terms of percentages of all Serious AEs collected from the time the subject signed the informed consent form until he/she stopped study participation.One subject randomized to receive MenACWY-CRM, received HepA/B+MenACWY-CRM vaccine, instead. The safety set included 85 subjects for HepA/B +MenACWY group and 83 for MenACWY.

Reporting Groups

	Description
HepA/B	Subject ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine.
HepA/B+ACWY	Subject ≥ 18 to ≤ 64 years of age who were not previously primed with hepatitis A and B vaccine received three doses of combined hepatitis A/B vaccine; subjects who were previously primed with combined hepatitis A/B received one booster dose; subjects who were previously primed with monovalent hepatitis B vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis B vaccine booster; first dose of hepatitis A vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis A vaccine; subjects who were previously primed with hepatitis A vaccine received one dose of combined hepatitis A/B vaccine on day 1 (hepatitis A vaccine booster; first dose of hepatitis B vaccine on an accelerated schedule), followed by two doses of monovalent hepatitis B vaccine; all the subjects concomitantly received one dose of MenACWY-CRM conjugate vaccine.
ACWY	Subject ≥ 18 to ≤ 64 years of age who received one dose of MenACWY-CRM conjugate vaccine.

Serious Adverse Events

	HepA/B	HepA/B+ACWY	ACWY
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/84 (1.19%)	0/85 (0%)	1/83 (1.2%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
RENAL CANCER *	1/84 (1.19%)	0/85 (0%)	0/83 (0%)
Psychiatric disorders			
COMPLETED SUICIDE *	0/84 (0%)	0/85 (0%)	1/83 (1.2%)

* Indicates events were collected by non-systematic methods.

Other Adverse Events

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

	HepA/B	HepA/B+ACWY	ACWY
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	25/84 (29.76%)	21/85 (24.71%)	12/83 (14.46%)
General disorders			
FATIGUE *	2/84 (2.38%)	6/85 (7.06%)	0/83 (0%)
INFLUENZA LIKE ILLNESS *	2/84 (2.38%)	1/85 (1.18%)	5/83 (6.02%)
INJECTION SITE PAIN *	4/84 (4.76%)	5/85 (5.88%)	1/83 (1.2%)
Infections and infestations			
NASOPHARYNGITIS *	6/84 (7.14%)	9/85 (10.59%)	5/83 (6.02%)
Nervous system disorders			
HEADACHE *	15/84 (17.86%)	6/85 (7.06%)	2/83 (2.41%)

* Indicates events were collected by non-systematic methods.

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

There is NOT an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

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