ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 04/09/2014

ClinicalTrials.gov ID: NCT00596271

Study Identification

Unique Protocol ID:	IC51-308
Brief Title:	Concomitant Vaccination With the Japanese Encephalitis Vaccine IC51 and HARVIX® 1440
Official Title:	Safety and Immunogenicity of Concomitant Vaccination With IC51 and HARVIX® 1440 in Healthy Subjects. A Single-blind Randomized, Controlled Phase 3 Study
Secondary IDs:	

Study Status

Record Verification:	April 2014
Overall Status:	Completed
Study Start:	September 2005
Primary Completion:	July 2006 [Actual]
Study Completion:	August 2008 [Actual]

Sponsor/Collaborators

Sponsor:	Valneva Austria GmbH
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? No

	Delayed Posting?
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CBER IND/IDE Number: 8589 Serial Number: 0034 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Germany: Paul-Ehrlich-Institut Austria: Agency for Health and Food Safety United States: Food and Drug Administration

Study Description

Brief Summary:	The objective is to investigate the immunogenicity of the Japanese Encephalitis vaccine IC51 (JE-PIV) single and concomitant with HAVRIX® 1440
Detailed Description:	This is a randomized, controlled, multi-center, single-blind phase 3 study. The study population consists of male and female healthy subjects, aged at least 18 years. 192 subjects will be enrolled at 2 sites in Europe.

Conditions

Conditions:	Japanese Encephalitis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Prevention
Study Phase:	Phase 3

Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Single Blind (Subject)
Allocation:	Randomized
Endpoint Classification:	Safety Study
Enrollment:	192 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: IC51 and Placebo 6 mcg i.m. IC51 with 2 injections (day 0 and 28)and placebo 0.5 mL with 1 injection (day 0)	Biological/Vaccine: IC51 Other Names: • Japanese Encephalitis purified inactivated vaccine Placebo
Active Comparator: HAVRIX and placebo HAVRIX with 1 injection (day 0) and placebo 0.5 mL with 2 injections (day 0 and 28)	Biological/Vaccine: HAVRIX Placebo
Active Comparator: IC51 and HAVRIX IC51 6 mcg i.m. with 2 injections (day 0 and 28) and HAVRIX with 1 injection (day 0)	Biological/Vaccine: IC51 Other Names: • Japanese Encephalitis purified inactivated vaccine Biological/Vaccine: HAVRIX

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	Yes
Criteria:	Inclusion Criteria: • At least 18 years of age

- In female subjects either childbearing potential terminated by surgery or one year post-menopausal, or a negative serum pregnancy test during screening and the willingness not to become pregnant during the study period and 30 days after the last vaccination by practicing reliable methods of contraception
- Written informed consent obtained prior to study entry

Exclusion Criteria:

- History of clinical manifestation of any flavivirus infection
- History of vaccination against Japanese encephalitis (JE), Yellow fever and Dengue fever (an anti-JEV neutralizing antibody titer >= 1:10 at baseline is acceptable for inclusion, these subjects will be part of the safety population, but will not be analyzed for immunogenicity in the per-protocol analysis)
- History of any previous Hepatitis A vaccination and infection
- Use of any other investigational or non-registered drug or vaccine in addition to the study vaccine during the study period or within 30 days preceding the first dose of study vaccine
- Planned administration of another vaccine during the study period
- Immunodeficiency including post-organ-transplantation or immunosuppressive therapy
- A family history of congenital or hereditary immunodeficiency
- History of autoimmune disease
- Administration of chronic (defined as more than 14 days) immunosuppressants or other immune-modifying drugs within six months of vaccination.
- Any acute infections within 4 weeks prior to enrollment
- Infection with human immunodeficiency virus (HIV), Hepatitis B (HBsAg) or Hepatitis C

Contacts/Locations

Study Officials: Astrid Kaltenboeck, Ph.D.
Study Director
Intercell AG

Locations:

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First Subject In: 26.09.2005, Last Subject Out: 14.07.2006 performed at centers for travelling medicine/ vaccinology

Reporting Groups

	Description
IC51 and Placebo	6 mcg i.m. IC51 with 2 injections (day 0 and 28)and placebo 0.5 mL with 1 injection (day 0)
HAVRIX and Placebo	HAVRIX with 1 injection (day 0) and placebo 0.5 mL with 2 injections (day 0 and 28)
IC51 and HAVRIX	IC51 6 mcg i.m. with 2 injections (day 0 and 28) and HAVRIX with 1 injection (day 0)

Overall Study

	IC51 and Placebo	HAVRIX and Placebo	IC51 and HAVRIX
Started	65	65	62
Completed	60	59	61
Not Completed	5	6	1

Baseline Characteristics

Reporting Groups

	Description
IC51 and Placebo	6 mcg i.m. IC51 with 2 injections (day 0 and 28)and placebo 0.5 mL with 1 injection (day 0)
HAVRIX and Placebo	HAVRIX with 1 injection (day 0) and placebo 0.5 mL with 2 injections (day 0 and 28)
IC51 and HAVRIX	IC51 6 mcg i.m. with 2 injections (day 0 and 28) and HAVRIX with 1 injection (day 0)

Baseline Measures

	IC51 and Placebo	HAVRIX and Placebo	IC51 and HAVRIX	Total
Number of Participants	65	65	62	192
Age, Categorical [units: participants]				
<=18 years	0	0	0	0

	IC51 and Placebo	HAVRIX and Placebo	IC51 and HAVRIX	Total
Between 18 and 65 years	65	65	62	192
>=65 years	0	0	0	0
Gender, Male/Female [units: participants]				
Female	34	35	34	103
Male	31	30	28	89
Region of Enrollment Europe [units: participants]	65	65	62	192

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Geometric Mean Titer (GMT) at Day 56 for Anti-JEV Neutralizing Antibodies
Measure Description	anti-JEV Neutralizing Antibodies were tabulated for IC51 groups only; for HAV GMTs (co-primary endpoint GMT for Hepatitis A Virus (HAV) Antibody at Day 28), please refer to "Outcome 2" within outcome measure section
Time Frame	Day 56
Safety Issue?	No

Analysis Population Description

Per Protocol Population includes all randomized subjects without major protocol deviations

Reporting Groups

	Description
IC51 and Placebo	
IC51 and HAVRIX	

Measured Values

	IC51 and Placebo	IC51 and HAVRIX
Number of Participants Analyzed	58	58
Geometric Mean Titer (GMT) at Day 56 for Anti-JEV Neutralizing Antibodies [units: titers] Geometric Mean (95% Confidence Interval)	192.2 (147.9 to 249.8)	202.7 (153.7 to 261.2)

Statistical Analysis 1 for Geometric Mean Titer (GMT) at Day 56 for Anti-JEV Neutralizing Antibodies

Statistical Analysis Overview	Comparison Groups	IC51 and Placebo, IC51 and HAVRIX
	Comments	The primary efficacy analysis will compare the IC51+HAVRIX vs. IC51+Placebo group in terms of the GMT for anti- JEV neutralizing antibody at day 56. An observed cases approach will be applied for the primary analysis
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority of the combined administration is postulated, if the lower bounds of both twosided 95% confidence intervals for the GMT ratios (of combined vaccination over single vaccination) are > 1/2. This procedure is equivalent to the approach based on a 1-sided test with a significance level of 2.5% for each comparison with the null hypothesis H0 : ratio ≤ 0.5 versus the alternative hypotheses H1 : ratio > 0.5.

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	GMT for Hepatitis A Virus (HAV) Antibody at Day 28
Measure Description	
Time Frame	Day 28
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
HAVRIX + Placebo	
IC51 + HAVRIX	

Measured Values

	HAVRIX + Placebo	IC51 + HAVRIX
Number of Participants Analyzed	52	58
GMT for Hepatitis A Virus (HAV) Antibody at Day 28 [units: titers] Geometric Mean (95% Confidence Interval)	21.7 (17.2 to 27.5)	24 (19.1 to 30.1)

Statistical Analysis 1 for GMT for Hepatitis A Virus (HAV) Antibody at Day 28

Statistical Analysis Overview	Comparison Groups	HAVRIX + Placebo, IC51 + HAVRIX
	Comments	The primary efficacy analysis will compare the IC51+HAVRIX vs. HAVRIX+Placebo group in terms of the GMT for HAV antibody at day 28. An observed cases approach will be applied for the primary analysis.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority of the combined administration is postulated, if the lower bounds of both twosided 95% confidence intervals for the GMT ratios (of combined vaccination over single vaccination) are > 1/2. This procedure is equivalent to the approach based on a 1-sided test with a significance level of 2.5% for each comparison with the null hypothesis H0 : ratio ≤ 0.5 versus the alternative hypotheses H1 : ratio > 0.5.

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Seroconversion Rate (SCR) at Day 56 for Plaque Reduction Neutralization Assay (PRNT) and HAV at Day 28
Measure Description	
Time Frame	day 28 and 56
Safety Issue?	No

Outcome Measure Data Not Reported

4. Secondary Outcome Measure:

Measure Title	GMT and SCR for PRNT at Day 28 and HAV at Day 56
Measure Description	
Time Frame	day 28 and 56
Safety Issue?	No

Outcome Measure Data Not Reported

5. Secondary Outcome Measure:

Measure Title	Safety
Measure Description	Rate of Adverse Events (AEs), Serious Adverse Events (SAEs) and medically attended AEs, local and systemic tolerability, changes in safety laboratory parameters (hematology, serum chemistry, urinalysis)
Time Frame	until 6 month after last vaccination
Safety Issue?	Yes

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
IC51 and Placebo	6 mcg i.m. IC51 with 2 injections (day 0 and 28)and placebo 0.5 mL with 1 injection (day 0)
HAVRIX and Placebo	HAVRIX with 1 injection (day 0) and placebo 0.5 mL with 2 injections (day 0 and 28)
IC51 and HAVRIX	IC51 6 mcg i.m. with 2 injections (day 0 and 28) and HAVRIX with 1 injection (day 0)

Serious Adverse Events

	IC51 and Placebo		HAVRIX and Placebo		IC51 and HAVRIX	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	1/65 (1.54%)		0/65 (0%)		0/62 (0%)	
Nervous system disorders						

	IC51 and Placebo		HAVRIX and Placebo		IC51 and HAVRIX	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Convulsion	1/65 (1.54%)	1	0/65 (0%)	0	0/62 (0%)	0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 2%

	IC51 and Placebo		HAVRIX and Placebo		IC51 and HAVRIX	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	27/65 (41.54%)		31/65 (47.69%)		24/62 (38.71%)	
Ear and labyrinth disorders						
Vertigo	1/65 (1.54%)		1/65 (1.54%)		2/62 (3.23%)	
Gastrointestinal disorders						
Diarrhea	1/65 (1.54%)		1/65 (1.54%)		4/62 (6.45%)	
Nausea	2/65 (3.08%)		2/65 (3.08%)		2/62 (3.23%)	
General disorders						
Fatique	2/65 (3.08%)		5/65 (7.69%)		5/62 (8.06%)	
Influenza like illness	6/65 (9.23%)		3/65 (4.62%)		3/62 (4.84%)	
Pyrexia	2/65 (3.08%)		0/65 (0%)		2/62 (3.23%)	
Infections and infestations						
Bronchitis	1/65 (1.54%)		0/65 (0%)		2/62 (3.23%)	
Cystitis	1/65 (1.54%)		1/65 (1.54%)		2/62 (3.23%)	
Gastrointeritis	0/65 (0%)		1/65 (1.54%)		2/62 (3.23%)	
Nasopharyngitis	4/65 (6.15%)		4/65 (6.15%)		5/62 (8.06%)	
Rash pustular	0/65 (0%)		2/65 (3.08%)		0/62 (0%)	
Rhinitis	2/65 (3.08%)		0/65 (0%)		2/62 (3.23%)	
Investigations						
Hepatic enzyme increased	2/65 (3.08%)		1/65 (1.54%)		0/62 (0%)	

	IC51 and Placebo		HAVRIX and Placebo		IC51 and HAVRIX	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Musculoskeletal and connective tissue disorders						
Myalgia	0/65 (0%)		1/65 (1.54%)		2/62 (3.23%)	
Nervous system disorders						
Headache	4/65 (6.15%)		10/65 (15.38%)		4/62 (6.45%)	
Respiratory, thoracic and mediastinal disorders						
Pharyngolaryngeal pain	3/65 (4.62%)		2/65 (3.08%)		0/62 (0%)	

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

There IS 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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