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Completed

ZIKA Vaccine in Naive Subjects

ClinicalTrials.gov ID **NCT02952833**

Sponsor National Institute of Allergy and Infectious Diseases (NIAID)

Information provided by National Institute of Allergy and Infectious Diseases (NIAID) (Responsible Party)

Last Update Posted 2018-12-07

Record History Tab

Study Record Versions

- This table shows all the versions of this study record arranged in order by submitted date.
  - To view one version of the study record, click the submitted date.
  - To compare two versions, select them using the check boxes and click "Compare" at the bottom of the list.

☐	1	2016-11-01	• None (earliest version on record)

Compare

Feedback

Valneva, Ex. 1031

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☐	3	2017-01-05	• Study Status • Study Description • Eligibility
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☐	9	2017-07-06	• Study Status • Study Design
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☐	16	2018-11-15	• Study Status
☐	17	2018-11-21	• Study Status
	Version	**Date submitted (YYYY-MM-DD)**	**Changes**

Version	**Date submitted (YYYY-MM-DD)**	**Changes**

*** Some sections** can only be displayed in Merged View.

Merged View **Side by Side**

Version 8: 2017-06-29 Version 10: 2017-09-14

Study Details

Study Identification

Unique Protocol ID
16-0033

Brief Title
ZIKA Vaccine in Naive Subjects

Official Title
Phase 1, Double-blinded, Placebo-Controlled Study of the Safety and Immunogenicity of Alum Adjuvanted Zika Virus Purified Inactivated Vaccine (ZPIV) Administered by the Intramuscular Route in Flavivirus Naïve Adult Subjects

Secondary IDs
HHSN272200800003C

Study Status

Record Verification
2017-~~04~~ 06-27

Overall Status
Recruiting

Version	Date submitted (YYYY-MM-DD)	Changes

Primary Completion
2018-01-15 [Estimated]

Study Completion
2018-10-02 [Estimated]

First Submitted
2016-10-13

First Submitted that Met QC Criteria
2016-11-01

First Posted
2016-11-02 [Estimated]

Last Update Submitted that Met QC Criteria
2017-~~06~~ 09-~~29~~ 14

Last Update Posted
2017-~~07~~09-~~02~~15 [Actual]

Sponsor/Collaborators

Sponsor
National Institute of Allergy and Infectious Diseases (NIAID)

Responsible Party
Sponsor

Collaborators

Oversight

U.S. FDA-regulated Drug
Yes

U.S. FDA-regulated Device
No

Product manufactured in and exported from the U.S
No

Data Monitoring

Study Description

Brief Summary
This study is a study to evaluate the safety of ZPIV. Three dose levels may be evaluated. The entire duration of each subject's participation is approximately 14 months including recruitment

and collection of data on the safety and reactogenicity of the study vaccine and samples for the assessment of immunogenicity. This study is expected to take approximately 30 months to complete from initiation through availability of a final report on the primary outcomes of safety and the secondary outcomes of humoral immunity to ZIKV. The Primary objectives of this study are to 1. Assess the safety and reactogenicity of a homologous prime boost regimen of ZPIV given at three different dose levels and 2. Compare the safety and reactogenicity profile of ZPIV after each vaccination and between dosage groups.

Detailed Description

This study is a single-center, double-blinded, placebo-controlled, Phase 1 study to evaluate the safety, reactogenicity, and immunogenicity of ZPIV administered in a homologous prime-boost regimen to Flavivirus-naïve healthy male and non-pregnant female adult subjects. Three dose levels may be evaluated: 5.0 mcg, 2.5 mcg and 10mcg of ZPIV. Each subject will receive either placebo or ZPIV administered by intramuscular (IM) injection on Days 1 and 29. The study will consist of a screening period of up to 28 days, a vaccination period in which subjects will receive a prime dose of vaccine on Day 1 followed by a boost on Day 29, and a follow-up period of 12 months post boost vaccination. The entire duration of each subject's participation is approximately 14 months including recruitment and collection of data on the safety and reactogenicity of the study vaccine and samples for the assessment of immunogenicity. This study is expected to take approximately 30 months to complete from initiation through availability of a final report on the primary outcomes of safety and the secondary outcomes of humoral immunity to ZIKV. The Primary objectives of this study are to 1. Assess the safety and reactogenicity of a homologous prime boost regimen of ZPIV given at three different dose levels, and 2. Compare the safety and reactogenicity profile of ZPIV after each vaccination and between dosage groups. The secondary objectives of this study are to 1. Assess the humoral immune response overall and by dosage group to a homologous prime-boost regimen of ZPIV as determined by kinetics of the immune responses, seroconversion rates, and peak Geometric Mean Titer (GMT) and to 2. Assess the durability of the humoral immune response overall and by dosage group to ZPIV at 6 and 12 months after the second vaccine administration.

Conditions

Condition
Zika Virus Infection

Keywords
Inactivated Phase I placebo-controlled Vaccine ZIKA

Study Design

Study Type
Interventional

Primary Purpose
Prevention

Study Phase
Phase 1

Interventional Study Model
~~Parallel Assignment~~ Sequential Assignment

Number of Arms
3

Masking
Double (Participant, Investigator)

Allocation
Randomized

Enrollment
90 [Estimated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Group 1 5.0 mcg ZPIV will be administered in a homologous prime-boost regimen on Day 1 and Day 29, n=25 (2 Sentinel subjects will receive intervention prior to remaining 23 subjects), Placebo for 5 subjects	Drug: Saline • Sodium chloride solu Biological: Zika Virus Purifie Inactivated Vaccine (ZPIV) • Zika Virus Purified Inactivated Vaccine v aluminum hydroxide adjuvant.
Experimental: Group 2 2.5 mcg ZPIV will be administered in a homologous prime-boost regimen on Day 1 and Day 29, n=25, Placebo for 5 subjects	Drug: Saline • Sodium chloride solu Biological: Zika Virus Purifie Inactivated Vaccine (ZPIV) • Zika Virus Purified Inactivated Vaccine v aluminum hydroxide adjuvant.
Experimental: Group 3 10 mcg of ZPIV will be administered in a homologous prime-boost regimen on Day 1 and Day 29, n=25, (2 Sentinel subjects will receive intervention prior to remaining 23 subjects) Placebo for 5 subjects	Drug: Saline • Sodium chloride solu Biological: Zika Virus Purifie Inactivated Vaccine (ZPIV) • Zika Virus Purified Inactivated Vaccine v aluminum hydroxide adjuvant.

Outcome Measures

Primary Outcome Measures

1. Comparison between dosage groups of the duration of vaccine-related Grade 2 or greater local or systemic reactogenicity
   [Time Frame: 8 Days after each vaccination]
2. Comparison between dosage groups of the duration overall and in each dosage group of vaccine-related Grade 3 local, systemic, or laboratory AE
   [Time Frame: 8 Days after each vaccination]
3. Comparison between dosage groups of the frequency of vaccine-related Grade 2 or greater local or systemic reactogenicity
   [Time Frame: 8 Days after each vaccination]
4. Comparison between dosage groups of the frequency of vaccine-related Grade 3 local, systemic, or laboratory AE
   [Time Frame: 8 Days after each vaccination]
5. Comparison between dosage groups of the type of vaccine-related Grade 2 or greater local or systemic reactogenicity
   [Time Frame: 8 Days after each vaccination]
6. Comparison between dosage groups of the type overall and each dosage group of vaccine-related Grade 3 local, systemic, or laboratory AE
   [Time Frame: 8 Days after each vaccination]
7. Comparison of study withdrawals, and discontinuation of study vaccination due to any reason between dosage groups.
   [Time Frame: 14 Months]
8. Duration overall and in each dosage group of serious adverse events (SAE) and adverse events of special interest (AESI) considered related to study vaccination
   [Time Frame: 14 Months]
9. Frequency of new onset chronic medical conditions
   [Time Frame: 14 Months]
10. Frequency overall and in each dosage group of serious adverse events (SAE) and adverse events of special interest (AESI) considered related to study vaccination
    [Time Frame: 14 Months]

11. Frequency overall and in each dosage group of solicited injection site and systemic reactogenicity.
[Time Frame: Day of vaccine administration to day 8 after each vaccination]
12. Frequency overall and in each dosage group of unsolicited vaccine-related adverse events (AE), including vaccine-related laboratory AE.
[Time Frame: 28 Days after each vaccination]
13. Severity overall and in each dosage group of solicited injection site and systemic reactogenicity.
[Time Frame: Day of vaccine administration to day 8 after each vaccination]
14. Severity overall and in each dosage group of unsolicited vaccine-related adverse events (AE), including vaccine-related laboratory AE.
[Time Frame: 28 Days after each vaccination]
15. Type overall and in each dosage group of serious adverse events (SAE) and adverse events of special interest (AESI) considered related to study vaccination
[Time Frame: 14 Months]

Secondary Outcome Measures

1. Peak GMT overall and by dosage group as measured by ZIKV ELISA and neutralization assay.
[Time Frame: At all post-vaccination visits, an average of 14 months]
2. Per visit GMT overall and by dosage group as measured by ZIKV ELISA and neutralization assay.
[Time Frame: At all post-vaccination visits, an average of 14 months]
3. Proportion of subjects overall and by dosage group that seroconvert to ZIKV at each post-vaccination visit by assessing ELISA responses in comparison with baseline
[Time Frame: At all post-vaccination visits, an average of 14 months]
4. Proportion of subjects overall and by dosage group that seroconvert to ZIKV at each post-vaccination visit by assessing neutralization titers in comparison with baseline
[Time Frame: At all post-vaccination visits, an average of 14 months]

Eligibility

Minimum Age

18 Years

Maximum Age

49 Years

Sex

All

Gender-based Eligibility

Gender Eligibility Description

Accepts Healthy Volunteers

Yes

Criteria

Inclusion Criteria:

1. Must be a male or non-pregnant, non-breastfeeding female between the age of 18 and 49 years, inclusive at the time of screening and enrollment
2. Must be willing and able to read, sign and date the informed consent document before study related procedures are performed
3. Must be willing and able to comply with study requirements and available for follow-up visits for the entire study
4. Must have a means to be contacted by telephone
5. Must have a body mass index (BMI) >/=18.1 and <35.0 kg/m^2
6. Must have acceptable* screening laboratory findings within 28 days before enrollment
    - Acceptable clinical laboratory parameters include:

- Hemoglobin: women: >11.5 g/dL; men >12.5 g/d
- White blood cell count: >3,400 cells/mm^3 but <11,000 cells/mm^3
- Platelets: >139,000 but <450,000 per mm^3
- Urine dipstick (clean urine sample): protein <1+, glucose negative
- Serum creatinine </=1 x institutional upper limit of normal (ULN)
- Blood urea nitrogen (BUN) <25
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <1.25 x institutional ULN
- Total bilirubin <1.25 x institutional ULN

- Note: If laboratory screening tests are out of acceptable range, repeat of screening tests is permitted once, provided there is an alternative explanation for the out of range value

7. Must be in good health based on the investigator's clinical judgment when considering findings from past medical history, medication use, vital signs, and an abbreviated physical examination.

Note 1: Good health is defined by the absence of any medical condition described in the exclusion criteria in a subject with a normal abbreviated physical exam and vital signs. If the subject has a preexisting condition not listed in exclusion criteria, it cannot meet any of the following criteria: 1) first diagnosed in last 3 months , 2) worsening in terms of clinical outcome in last 6 months; or 3) involves need for medication that may pose a risk to subject's safety or impede assessment of adverse events or immunogenicity if they participate in study Note 2: An abbreviated physical exam differs from a complete exam in that it does not include a genitourinary and rectal exam.

Note 3: Vital signs must be normal by protocol toxicity grading scale or determined to be normal-variant by investigator. In the event of an abnormal heart rate or blood pressure due to physiological variation or activity, the subject may rest for 10 minutes in a quiet room, and then blood pressure and/or heart rate may be re-measured. Repeated vital signs may be used to determine eligibility 8. Women of childbearing potential* must have a negative serum pregnancy test at screening and a

negative urine pregnancy test immediately prior to each vaccination

- Note: All female subjects are considered of childbearing potential unless postmenopausal or surgically sterilized and >/=3 months have passed since sterilization procedure. Postmenopausal is defined as amenorrhea for >/=12 months without an alternative medical cause. Permanent female sterilization procedures include tubal ligation, bilateral salpingectomy, hysterectomy, bilateral oophorectomy, or successful Essure placement.

  9. Women of childbearing potential must use an acceptable method of contraception* from one month (30 days) prior to the first vaccination until at least 60 days after the last vaccination.

- Acceptable methods of contraception include the following:

  - Use highly effective contraceptive methods, defined by <1% failure rate per year independent of user adherence, including long-acting reversible contraception (LARC): progestin-releasing subdermal implants and intrauterine devices (IUD), OR
  - Use effective contraceptive methods, defined by 5-9% failure rate with typical use and <1% failure rate with consistent and correct use, including:

prescription oral contraceptives, contraceptive injections, combined pill, progestin-only pill, hormone-releasing transdermal patch or vaginal ring, and depot medroxyprogesterone acetate injection (Depo-Provera), OR

- Male sex partners must have had a vasectomy >/=3 months prior to first vaccination, OR
- Practice abstinence defined as refraining from heterosexual intercourse from 30 days before first vaccination until at least 60 days after 2nd vaccination 10. Female subjects must agree to not donate eggs (ova, oocytes) from the start of screening period until at least 60 days after receiving the last vaccination 11. Subjects must provide concurrent consent at the time of enrollment

and 1st vaccination to future use of stored blood samples to measure immunity to ZIKV

Exclusion Criteria:

1. Has plans to become pregnant during the course of the study, or is currently pregnant or breastfeeding.
2. Has plans to travel to an area with active Zika virus, DENV, YFV or JEV transmission* during the study or returned from travel to an area with active transmission* within 30 days of screening.

   * NOTE: Refer to CDC website for areas with active Zika, DENV, YFV, or JEV virus transmission: http://www.cdc.gov

3. Has history of vaccination with a licensed or investigational flavivirus vaccine* or reportedly diagnosed with a flavivirus infection or disease.
   - Includes subject's verbal history of vaccination or disease with any of the following flaviviruses:
     - Yellow Fever virus (YFV): YF-VAX, Stamaril, or Bio-Manguinhos YF vaccine
     - Japanese encephalitis virus (JEV): investigational vaccine or licensed vaccine (IXIARO)
     - Dengue virus (DENV): investigational vaccine or Sanofi Pasteur newly licensed vaccine
     - West Nile virus (WNV): investigational vaccine
     - Zika virus (ZIKV)
     - Other: St. Louis encephalitis, or tick-borne encephalitis virus (TBEV)
4. Plans to receive a licensed flavivirus vaccine or participate in another flavivirus vaccine trial during the study.
5. Has positive serology to DENV, ZIKV, YFV, or WNV*.
   - Serologic tests must be performed within 60 days of enrollment
6. Has positive serology for HIV 1/2, Hepatitis C virus, or Hepatitis B surface antigen*.
   - Serologic tests must be performed within 60 days of enrollment

7. Has known or suspected congenital or acquired immunodeficiency, or recent history or current use of immunosuppressive therapy.*
    - Anti-cancer chemotherapy or radiation therapy within the preceding 6 months, or long-term (at least 2 weeks within the previous 3 months) systemic corticosteroids therapy (at a dose of at least 0.5 mg/kg/day). Intranasal or topical prednisone (or equivalent) is allowed.
8. Had organ and/or stem cell transplantation whether or not on chronic immunosuppressive therapy.
9. Has history of malignancy other than squamous cell or basal cell skin cancer, unless there has been surgical excision that is considered to have achieved cure*.
    - Subjects with a history of skin cancer must not be vaccinated at the previous tumor site
10. Has history of chronic or acute severe neurologic condition*.
    - Including history of Guillain-Barre syndrome, seizure disorder or epilepsy, Bell's palsy, meningitis, or disease with any focal neurologic deficits
11. Has diabetes mellitus type 1 or type 2, including cases controlled with diet alone.

    Note: history of isolated gestational diabetes is not an exclusion criterion.

12. Has history of thyroidectomy, or thyroid disease requiring medication during the last 12 months.
13. Has major psychiatric illness during last 12 months that in the investigator's opinion would preclude participation.
14. Has history of other chronic disease or condition*
    - Includes the conditions and diagnoses defined as AESI in section 9, as well as autoimmune disease, hypercholesterolemia, chronic hepatitis or cirrhosis, chronic pulmonary disease, chronic renal disease, and chronic cardiac disease including hypertension even if medically controlled
        - Vital signs must be normal by protocol toxicity grading scale or determined to be

normal-variant by investigator. In the event of an abnormal heart rate or blood pressure due to physiological variation or activity, the subject may rest for 10 minutes in a quiet room, and then blood pressure and/or heart rate may be re-measured. Repeated vital signs may be used to determine eligibility.

15. Has current or past history of substance abuse that in the investigator's opinion would preclude participation.
16. Has tattoos, scars, or other marks on the deltoid areas that would, in the opinion of the investigator, interfere with assessment of the vaccination site(s)
17. Has a history of chronic urticaria (recurrent hives).
18. Has known allergy or history of anaphylaxis or other serious reaction to a vaccine or vaccine component*.
    - Including aluminum hydroxide (alum) or aminoglycosides (e.g., neomycin and streptomycin).
19. Had major surgery (per the investigator's judgment) in the month prior to screening or plans to have major surgery during the study.
20. Received blood products or immunoglobulin in the 3 months prior to screening or planned use during the course of the study.
21. Donated a unit of blood within 8 weeks before Day 1 or plans to donate blood during the course of the study.
22. Received live attenuated vaccine from 30 days before Day 1 until 30 days after the last vaccination.
23. Received killed or inactivated vaccine from 14 days before Day 1 until 14 days after the last vaccination.
24. Received experimental therapeutic agents within 3 months prior to the first study vaccination or plans to receive any experimental therapeutic agents during the course of the study.
25. Is currently participating or plans to participate in another clinical study involving an investigational product, blood drawing, or an invasive procedure listed below*.
    - An invasive procedure requiring administration of anesthetics or intravenous dyes or removal of tissue would be excluded. This includes endoscopy, bronchoscopy, or administration of IV contrast.
26. Has an acute illness or temperature >/=38.0ºC on Day 1 or Day 29* or within 2days prior*.

- Subjects with fever or an acute illness on the day of vaccination or in the 2 days prior to vaccination may be re-assessed and enrolled if healthy or only minor residual symptoms remain within 2 days of Day 1 or Day 29.

27. Is a study site employee* or staff paid entirely or partially by the OCRR contract for the trial, or staff who are supervised by the PI or Sub-Investigators.
    - Including the Principal Investigator, sub-Investigators listed in Form FDA 1572 or Investigator of Record Form
28. In the investigator's opinion, the subject cannot communicate reliably, is unlikely to adhere to the study requirements, or has a condition that would limit their ability to complete the study.

Contacts/Locations

Central Contact Person

- Name
  Sarah L George

  Telephone
  13149779035

  Email
  georgesl@slu.edu

Study Officials

Location

- **Saint Louis, Missouri, United States, 63104-1015**
  Status:
  Recruiting

  Facility:
  Saint Louis University - Center for Vaccine Development

IPD Sharing

IPD information

References

Citations

Links

Available IPD/Information

Document Section