A PHASE 3, MULTICENTER, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLINDED TRIAL TO EVALUATE THE EFFICACY, SAFETY, TOLERABILITY, IMMUNOGENICITY, AND LOT CONSISTENCY OF A 6-VALENT OspA-BASED LYME DISEASE VACCINE IN HEALTHY PARTICIPANTS >=5 YEARS OF AGE

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This study has been transitioned to CTIS with ID 2023-509105-72-00 check the CTIS register for the current data. * To demonstrate the efficacy of VLA15 in preventing confirmed Lyme disease in the Lyme disease season after completion of the primary...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56314

Source
ToetsingOnline

Brief title
VALOR

Condition

- Other condition
- Bacterial infectious disorders

Synonym
Lyme disease and tick fever

Health condition

Lyme disease caused by Borrelia species

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer Inc

Intervention

Keyword: Lyme disease, Phase 3, Vaccine

Outcome measures

Primary outcome

Primary Efficacy:

Clinically- and laboratory-confirmed Lyme disease caused by B burgdorferi sensu

lato (as determined by the AC).

VE, defined as the relative risk reduction of the clinically- and

laboratory-confirmed Lyme disease cases in the VLA15 group compared to the

placebo group, from 28 days after receiving the booster dose through the end

of the Lyme disease season following the booster dose (end of October), and in

compliance with the key protocol criteria (evaluable efficacy population).

Primary Safety:

* Local reactions (pain at the injection site, redness, and swelling).

* Systemic events (fever, headache, fatigue, muscle pain, and joint pain).

* AEs.

* NDCMCs.

* SAEs.

Primary Immunogenicity (Lot-Consistency Subset):

Anti-OspA quantitative immunological assay titer.

In participants receiving all primary series and booster dose of 3 different lots of vaccine in compliance with the key predefined criteria.

Secondary outcome

Secondary Efficacy:

* Clinically- and laboratory-confirmed Lyme disease caused by B burgdorferi sensu lato (as determined by the AC).

VE, defined as the relative risk reduction of the clinically- and laboratory-confirmed Lyme disease cases in the VLA15 group compared to the placebo group, from 28 days after receiving the booster dose through the end of the Lyme disease season following the booster dose (end of October), and in compliance with the key protocol criteria among participants enrolled from NA sites (evaluable efficacy population).

*Clinically- and laboratory-confirmed Lyme disease caused by B burgdorferi sensu lato (as determined by the AC).

VE, defined as the relative risk reduction of the clinically- and laboratory-confirmed Lyme disease cases in the VLA15 group compared to the

placebo group, from 28 days after completing the primary series through the end

of the Lyme disease season following the primary series (end of October), and

in compliance with the key protocol criteria (evaluable efficacy population).

Study description

Background summary

Lyme disease is the most prevalent vector-borne disease in humans across the temperate regions of the northern hemisphere. Hundreds of thousands of people in NA (US and Canada) and Eurasia are affected annually. Lyme disease can occur at any age; however, incidence peaks in children 5 to 15 years of age and adults >50 years of age.

Infections can occur throughout the year but primarily occur from the midspring through summer months as these are the time periods when nymphal ticks seek hosts for a blood meal and when humans are most likely to enter tick habitats. Human proximity to tick habitats such as forested and shrub areas increases the likelihood of infection as well as occupations such as forestry and hobbies such as hunting and hiking in Lyme-endemic regions.

Lyme disease is caused by bacteria Borrelia burgdorferi which transmits to humans during tick feeding when the Borrelia spirochetes migrate out of the tick midgut and into the bite site, a process that occurs approximately 36 to 48 hours after attachment. The most common clinical manifestation of Lyme disease is a gradually expanding erythematous skin rash known as erythema migrans (EM). EM appears within days to weeks (average ~1 to 2 weeks) at the location of a tick bite and is often accompanied by symptoms of fatigue, fever, headache, mild stiffness of the neck, arthralgia, or myalgia. If untreated or inadequately treated with antibiotics, the infection can disseminate via the bloodstream to other parts of the body, where it can cause serious manifestations affecting the nervous system (neuroborreliosis presenting as facial palsy, meningitis, myelitis, or encephalitis), joints (recurrent or persistent large joint synovitis), or heart (conduction abnormalities and carditis).

In practice, personal preventive measures have had minimal impact on the incidence of Lyme disease. Unfortunately, people infected with Borrelia can become infected multiple times. As antibiotic therapy may not always be curative, and Lyme disease is increasing in incidence and spreading geographically, more reliable preventive measures, such as a vaccine, are needed to further help reduce the risk of acquiring this potentially

devastating disease.

Currently, there is no licensed human Lyme disease vaccine available, and no other human Lyme disease vaccine candidate is in active clinical development. To address this unmet medical need and based on successful proof-of-concept findings from prior OspA-based transmission-blocking vaccine studies, Pfizer and Valneva SE have partnered to codevelop a vaccine called VLA15, which will be investigated for the following indication:
Active immunization for the prevention of Lyme disease in individuals 5 years of age and older.

Study objective

This study has been transitioned to CTIS with ID 2023-509105-72-00 check the CTIS register for the current data.

* To demonstrate the efficacy of VLA15 in preventing confirmed Lyme disease in the Lyme disease season after completion of the primary series vaccination and booster dose.
* To describe the safety profile of VLA15 as measured by the percentage of participants reporting local reactions, systemic events, AEs, NDCMCs, and SAEs.
* To demonstrate that the immune responses to the 6 serotypes induced by VLA15 are equivalent across 3 independent lots.
* To demonstrate that the immune responses to the 6 serotypes induced by VLA15 in children 5 through 17 years of age are noninferior to those in adults 18 through 44 years of age after the booster dose.
* To demonstrate the efficacy of VLA15 in preventing confirmed Lyme disease in the Lyme disease season after completion of the primary series vaccination and booster dose in NA.
* To demonstrate the efficacy of VLA15 in preventing confirmed Lyme disease in the Lyme disease season after completion of the primary series vaccination.
* To describe the efficacy of VLA15 in reducing otherwise undiagnosed Lyme disease seroconversion after each season.
* To describe the efficacy of VLA15 in preventing confirmed Lyme disease by geographic region (NA and Europe separately).
* To describe the immunogenicity for all vaccine serotypes after completion of the primary series vaccination and booster dose of VLA15.
* To describe the efficacy of VLA15 by serotype and risk factor.
* To describe the characteristics of participants diagnosed with PTLD that occurred in the Lyme disease season after completion of the primary series vaccination.

Study design

This is a Phase 3, multicenter, placebo-controlled, randomized, observer-blinded trial to evaluate the safety, efficacy, immunogenicity, and

lot consistency of a 6-valent OspA-based Lyme disease vaccine, VLA15, in healthy participants >=5 years of age. In the Netherlands, an application for approval is being submitted for the recruitment of the adult population. Randomization will occur after informed consent/assent and eligibility review and will be stratified by geographic region. For participants enrolled from European sites or Canadian sites, VLA15 from Lot 1 will be used and the randomization ratio will be 1:1 (VLA15 from Lot 1: placebo); for participant enrolled from US sites, VLA15 from 3 different lots will be used. The overall study randomization ratio between VLA15 and placebo will be maintained as 1:1.

This study is designed to demonstrate that a 3-dose extended-schedule primary vaccination series administered over ~5 to 9 months and a booster dose given prior to the start of the second season will protect against Lyme disease during the Lyme disease season following
the booster dose. The primary series will be completed from approximately April to as late as August 2023 for individuals enrolled between August 2022 and March 2023, and these participants will contribute to post-primary series case detection during the 2023 Lyme disease season and the postbooster case detection during the Lyme disease season in 2024.
For participants enrolled after March 2023, whose vaccinations will commence in July 2023, the primary series will be completed from early April to early May 2024, and these participants will contribute to post-primary series case detection during the 2024 Lyme disease season and postbooster case detection during the Lyme disease season in 2025. The primary series will be followed by a booster dose 1 year later, from approximately March to early May just prior to the beginning of the second Lyme disease season.

It is expected that each participant will participate in the study for up to 30 months.

All participants will be asked at Visit 1 and periodically reminded to present to their clinical sites for an unscheduled visit whenever experiencing symptoms associated with Lyme disease. If the investigator has a reasonable clinical suspicion of Lyme disease the unscheduled visit should be converted to a suspected-Lyme disease acute visit. Targeted PE will be performed and blood samples will be taken and tested for for the presence of borrelial infection.
If appropriate, a photograph(s) of pertinent Lyme disease-related findings will be taken. For participants presenting with skin manifestations suspicious for Lyme disease, a maximum of two 2-mm skin punch biopsy samples will be obtained for further laboratory testing following provision of supplemental consent. If other biological samples (ie, CSF/paired serum, synovial fluid) are obtained from a participant as a part of clinical care, sites will be asked to provide residual sample material to the sponsor. Treatment will be given on the basis of standard of care.

A suspected Lyme disease convalescent visit will occur approximately 1 month after the suspected-Lyme disease acute visit. At this visit, participants will

be assessed for resolution of their signs/symptoms, and an additional blood sample will be obtained.

A confirmed Lyme disease PTLD-assessment visit will occur approximately 9 to 12 months after completion of treatment for all EAC-confirmed Lyme disease cases identified in the Lyme disease season following the primary series only.

Intervention

Intervention Name: PF-07307405 (VLA15) (Vaccine) // Normal Saline (Placebo)
Unit dose strength: 0,5mL
Route of Administration: Intramuscular injection
IMP
Sourcing: Provided centrally by the sponsor
Packaging and labeling: Study intervention will be provided in pre-filled syringes (PFSs). Each PFS will be labeled as required per country requirement
Dosing:
Dose 1 (Start of Primary Series: Day 1)
Dose 2 (50-70 Days After Visit 1)
Dose 3 (End of Primary Series: 1-Month Period Prior to First Lyme Disease Season)
Booster Dose (2-Month Period Prior to Second Lyme Disease Season)

Study burden and risks

Common AEs noted after vaccination with the study intervention VLA15 are primarily related to reactogenicity, including local reactions (pain, tenderness, swelling, induration/hardening, itching, and erythema/redness around the injection site) and systemic events (headache, fatigue, myalgias, arthralgias, chills, fever, rash, and flu-like symptoms).
The safety profile is largely derived from Phase 2 studies.
As with any vaccine, an allergic reaction may occur. Symptoms of an allergic reaction can include swelling of the lips, mouth, and throat, which may cause difficulty in swallowing or breathing; skin rash; swelling of the hands, feet, and ankles; dizziness; and fainting. A severe allergic shock (anaphylactic shock) may occur.
Risks that may be associated with study procedures include risk from venipuncture blood sampling, such as feeling faint, dizziness, fainting, pain, swelling, bruising, and infection in the vicinity of the vein from where blood is taken. Risks associated with skin punch biopsies are the same as those for venipuncture in addition to scarring at the biopsy site, the possibility of requiring a suture, and allergic reaction (including anaphylaxis and death) to local anesthesia. There may also be additional risks associated with the vaccines administered during the study, which are unknown at this time.

Safety assessments described in this protocol and ongoing safety data reviews

by the investigator, the sponsor*s global medical monitor, the internal risk management committee, and the external DMC will serve to monitor and mitigate these risks.

OspA ST1-based vaccines have been shown to be protective against Lyme disease in humans previously in 2 independent efficacy studies, thus validating the mechanism and OspA target. VLA15 was effective in animal models and induced immune responses in the majority of study participants in Phase 1 and 2 studies. However, as VLA15 is a new multivalent construct that has not yet been tested for clinical efficacy, the participants might not directly benefit from vaccination with VLA15.

Benefits to individual participants include:
* Active surveillance for and access to evaluation and treatment of Lyme disease.
* Clinical assessment by a medical provider at the start of the study and at additional time points (disease visits) throughout the study.
* Evaluations and management of some illnesses (AEs) that occur during participation in the study
* Receipt of a vaccine that may potentially prevent Lyme disease.

Overall Benefit/Risk Conclusion
Taking into account the measures to minimize risk to study participants, the potential risks identified in association with VLA15 primarily include well-established local reactions and systemic events common to many vaccines and that are mostly mild to moderate in severity and transient in nature, or minor complications expected from procedures (vaccination, venipuncture, skin punch biopsy), and are justified by the anticipated benefits that may be afforded to healthy adult and pediatric participants.

Contacts

Public
Pfizer

Rivium Westlaan 142
Capelle a/d IJssel 2909LD
NL
Scientific
Pfizer

Rivium Westlaan 142
Capelle a/d IJssel 2909LD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1.Male or female participants >= 5 years of age at enrolment (younger population only recruited in countries that have received full regulatory approval).
Type of Participant and Disease Characteristics:
2.Participants who reside in areas with endemic Lyme disease and who lead lifestyles that put them at increased risk for Lyme disease.
3.Participants or participants' parent(s)/legal guardian(s), who are willing and able to comply with all scheduled visits, investigational plan, laboratory tests, lifestyle considerations, and other study procedures (younger population only recruited in countries that have received full regulatory approval).
4.Healthy male and female participants at enrollment
5.Capable of giving signed informed consent, and assent (as appropriate).

Exclusion criteria

1. Pregnant female participants. Participants unwilling or unable to use effective methods of contraception as outlined in this protocol from the signing of the informed consent through 28 days after completion of the primary vaccination series and from the booster dose through 28 days after the booster vaccination.
Medical Conditions:
2. Any contraindication to vaccination or vaccine components, including previous anaphylactic reaction to any vaccine or vaccine-related components.
3. Any diagnosis of Lyme disease within the past 3 months.
4. Any history of Lyme carditis, neuroborreliosis, arthritis, or other disseminated Lyme disease regardless of when diagnosed.
5. Known tick bite within the past 4 weeks.
6. Newly developed or unstable underlying conditions that may interfere with

the assessment of Lyme disease, including but not limited to chronic arthralgia/arthritis, second/third-degree AV heart block, chronic pain syndromes, and chronic skin conditions that reduce the ability to detect cutaneous manifestations of Lyme disease.
7. Underlying clotting deficiency (eg, bleeding disorder, thrombocytopenia) that may increase the risk of excessive bleeding following required study procedures.
8. Congenital or acquired immunodeficiency or treatments that would inhibit the ability to mount an immune response to a vaccine.
9. Any unstable autoimmune condition with a manifestation (eg, arthritic and neurologic) that may interfere with the assessment of Lyme disease (Potential participants with well-controlled, stable autoimmune conditions under the care of a rheumatologist are eligible).
10. Underlying bone marrow disorder such as myelodysplasia, myeloma, or myeloproliferative disorder, treated within the past year, or any history of bone marrow transplant.
11. Malignancy that required treatment with chemotherapy (including the use of adjunctive and hormonal therapy), immunotherapy, radiation therapy, or antineoplastic target therapies within the past 24 months.
12. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.
Prior/Concomitant Therapy:
13. Receipt of a previous vaccination for Lyme disease.
14. Treatment for Lyme disease in the 3 months prior to study intervention administration.
15. Chronic systemic doxycycline or minocycline or other tetracycline class drug use for acne or any other chronic suppressive antibiotics used to treat other conditions.
16. Receipt of blood/plasma products or immunoglobulins within 6 months before study intervention administration through conclusion of the study.
17. Receipt of systemic corticosteroids (>=20 mg/day of prednisone or equivalent) for >=14 days within 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted.
18. Receipt of chronic systemic treatment with other known immunosuppressant medications, or radiotherapy, within 6 months before study intervention administration.
19. Receipt of anticoagulant therapy within 1 month before study intervention administration.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-09-2022
Enrollment:	234
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	6-Valent OspA-Based Lyme Disease Vaccine

Ethics review

Approved WMO Date:	19-04-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-08-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-09-2022
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-10-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-11-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-03-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-06-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	15-08-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-10-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-12-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-06-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-08-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-509105-72-00
EudraCT	EUCTR2021-005427-20-NL
ClinicalTrials.gov	NCT05477524
CCMO	NL80806.000.22