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A PHASE 1 STUDY ASSESSING THE SAFETY, IMMUNOGENICITY AND DOSE-RESPONSE OF VLA15, A MULTIVALENT RECOMBINANT OSPA-BASED VACCINE CANDIDATE AGAINST LYME BORRELIOSIS, IN HEALTHY ADULTS AGED BELOW 40 YEARS

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BACKGROUND

Lyme borreliosis (LB) is the most common tick-borne disease caused by several genospecies of the spirochete *Borrelia burgdorferi sensu lato (B.b.s.l.)*. Increasing case numbers and a lack of effective preventive measures emphasize the need for a vaccine. OspA is a dominant surface protein expressed by the spirochetes while in the tick midgut and a proven target for a LB vaccine. VLA15 is a subunit vaccine candidate targeting the six most prevalent OspA serotypes (STs) that cause LB in Europe (OspA ST1-6) and the US (OspA ST1) (*Figure 1*).

Valneva conducted a first-in-human partially randomized, observer-blind, multi-centre Phase 1 study in healthy volunteers to assess the safety, immunogenicity and dose response of VLA15. Safety and immunogenicity of a booster dose applied 12–15 months after the first immunization were assessed in a subset of volunteers (*Figure 2*).

Figure 1: Valneva's Lyme Borreliosis Vaccine Candidate VLA15

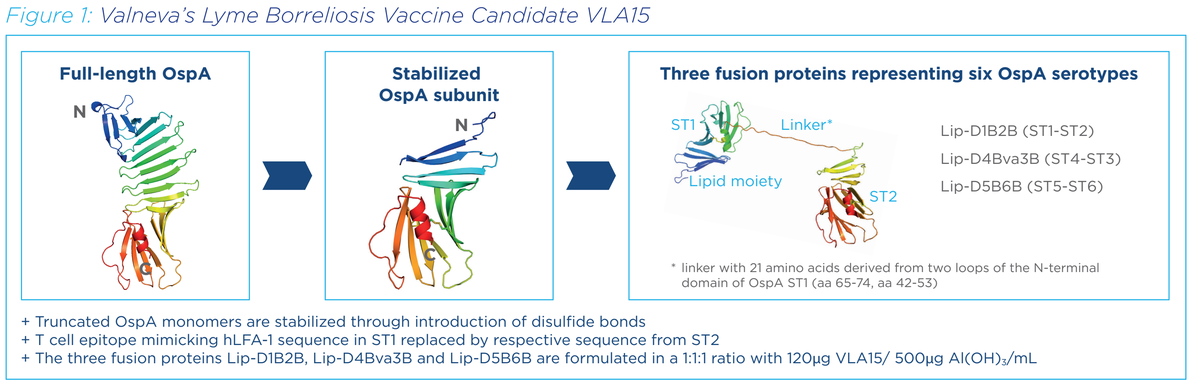
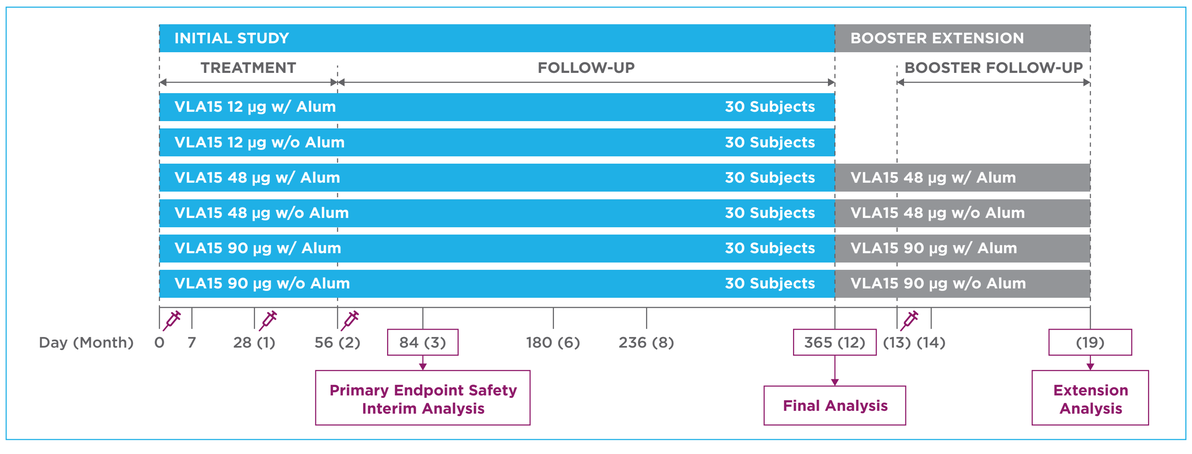


Figure 2: Study Design VLA15-101 – First-in-Human Study



METHODS

CLINICAL STUDY VLA15-101 – FIRST-IN-HUMAN STUDY

+ **Observer-blind, randomized, multi-center, dose-escalation study**
+ **Study Population:** 179 healthy volunteers aged 18 to 39 years, *B.b.s.l.* seronegative (C6 ELISA)
+ **Study Locations:** non-/low endemic regions in Belgium and US
+ **Primary objective:** Safety to Day 84
+ **Secondary objectives:** Safety to Month 12, Immunogenicity
+ **Exploratory objectives:** Safety and immunogenicity of a booster dose of VLA15 applied at 12-15 months after first immunization
+ **Safety assessment:** Solicited Adverse Events captured 7 days after each vaccination[1], unsolicited Adverse Events, SAEs
+ **Immunogenicity assessment:** ELISA against recombinant OspA from *B.b.s.l.* serotypes 1–6

RESULTS *SAFETY*

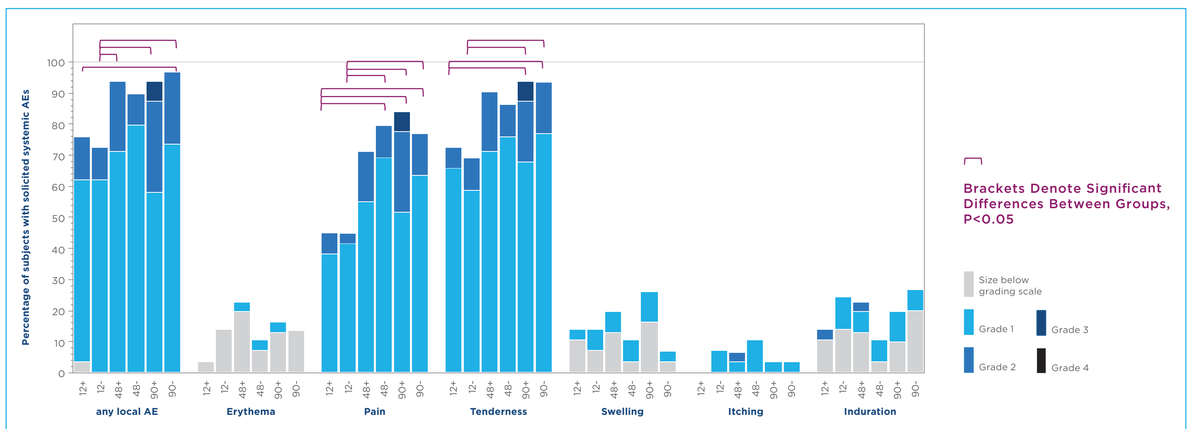
Table 1: Overview of Adverse Events up to Day 84 (Primary Endpoint)

OVERALL Subjects with at least one	12 µg + Alum N=29 n (%)	12 µg - Alum N=29 n (%)	48 µg + Alum N=31 n (%)	48 µg - Alum N=29 n (%)	90 µg + Alum N=31 n (%)	90 µg - Alum N=30 n (%)	Pooled VLA15 N=179 n (%)
AE	25 (86.2)	25 (86.2)	30 (96.8)	28 (96.6)	29 (93.5)	29 (96.7)	166 (92.7)
Solicited AE	24 (82.8)	25 (86.2)	30 (96.8)	27 (93.1)	29 (93.5)	29 (96.7)	164 (91.6)
Unsolicited AE	14 (48.3)	17 (58.6)	19 (61.3)	13 (44.8)	14 (45.2)	16 (53.3)	93 (52.0)
Related AE	24 (82.8)	25 (86.2)	30 (96.8)	28 (96.6)	29 (93.5)	29 (96.7)	165 (92.2)
Severe*, related AE[a]	0 (0.0)	1 (3.4)	1 (3.2)	1 (3.4)	3 (9.7)	2 (6.7)	8 (4.5)
Related, unsol. AE	3 (10.3)	7 (24.1)	4 (12.9)	3 (10.3)	2 (6.5)	3 (10.0)	22 (12.3)
Serious AE[b] (No related SAEs)	1 (3.4)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)

No Arthritis, Rheumatoid Arthritis or AEs potentially associated with LB were observed during entire study

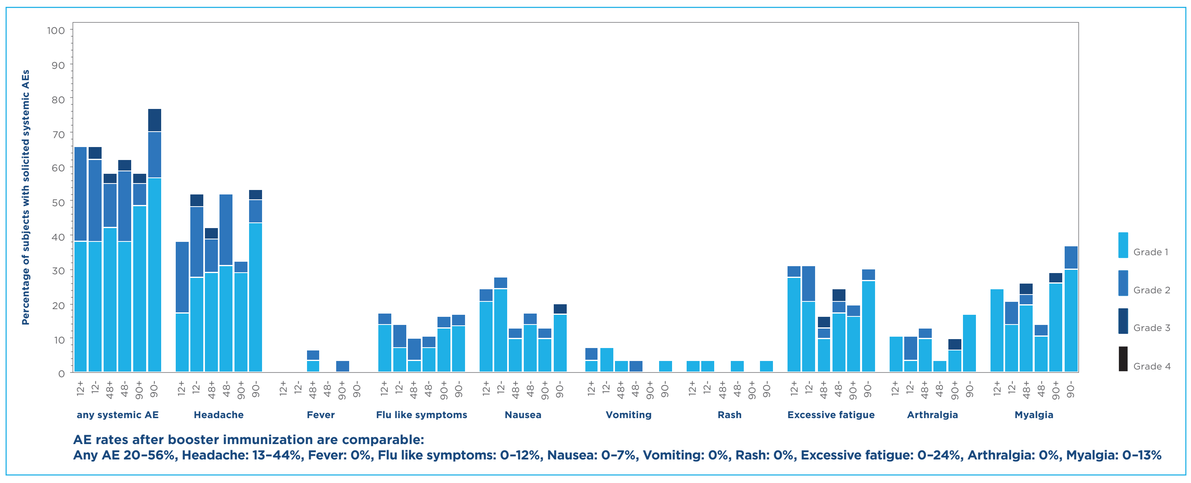
* Grade 3 or 4; a) All severe related AEs were solicited AEs; b) Spinal fracture, Hypoaesthesia

Figure 3: Solicited Local Adverse Events, Safety Population



AE rates after booster immunization are comparable:
Any AE: 56–100%, Erythema: 0–20%, Pain: 38–77%, Tenderness: 56–94%, Swelling 0–13%, Itching 0%, Induration 12–20%

Figure 4: Solicited Systemic Adverse Events, Safety Population



AE rates after booster immunization are comparable:
Any AE 20–56%, Headache: 13–44%, Fever: 0%, Flu like symptoms: 0–12%, Nausea: 0–7%, Vomiting: 0%, Rash: 0%, Excessive fatigue: 0–24%, Arthralgia: 0%, Myalgia: 0–13%

RESULTS *IMMUNOGENICITY*

Figure 5: GMT for OspA Serotypes 1-6 specific IgG, Day 84, PP population

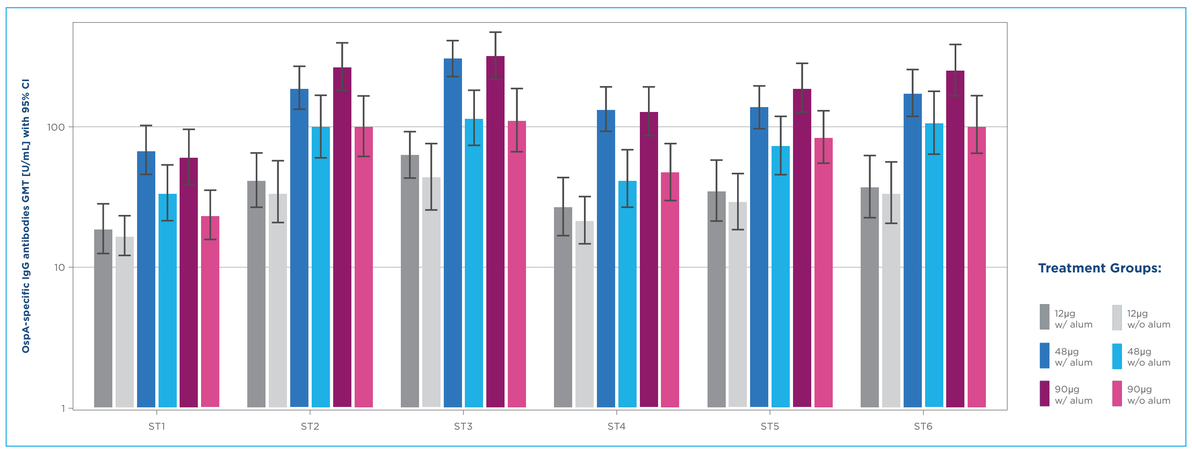
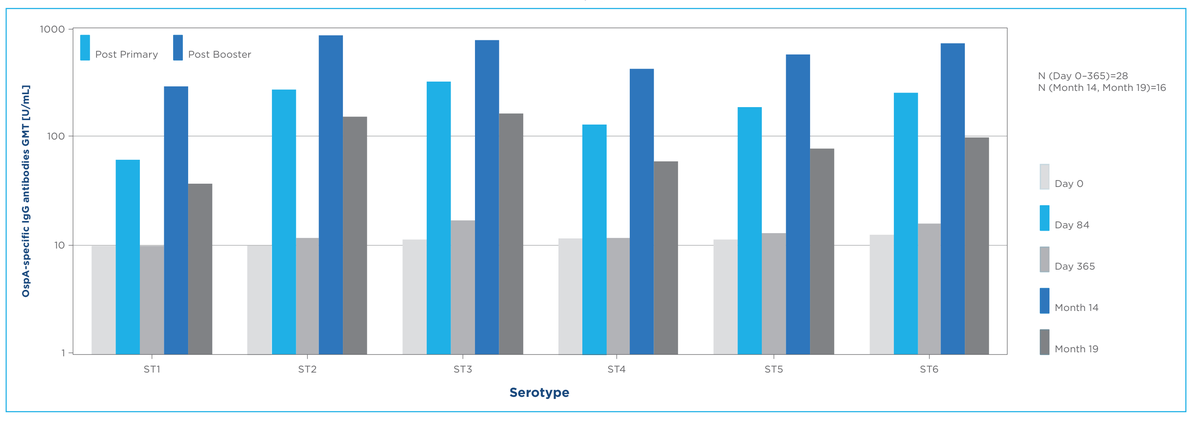


Figure 6: GMT for OspA Serotypes 1-6 specific IgG, 90 µg with Alum Group, over Time, PP population



CONCLUSIONS

+ VLA15 was safe and well tolerated in all treatment groups with no associated safety concerns during the entire study, including the booster.
+ AE rates are comparable to licensed lipidated or lipid containing protein vaccines (e.g. Trumenba[2], Bexsero[3]).
+ VLA15 was immunogenic in all doses and formulations tested, i.e. IgG antibody responses were seen in all groups with superior immunogenicity in adjuvanted treatment groups and in the higher dose groups.
+ A substantial booster effect of VLA15 could be observed in all treatment groups that received booster immunization.

OUTLOOK

+ Serum Bactericidal Assays are currently being developed to gain information on functionality of antibodies.
+ VLA15 is currently tested in two Phase 2 studies evaluating higher doses of VLA15 w/ alum (135 µg, 180 µg) and two immunization schedules (Month 0-1-2 and Month 0-2-6).

References: *1) Toxicity Grading Scale for Healthy Adult and Adolescent Subjects Enrolled in Preventive Vaccine Trials (2007). 2) Trumenba Highlights of prescribing information 9/2017. 3) Bexsero Highlights of prescribing information 10/2017.*