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Safety and Immunogenicity of mRNA-1982 and mRNA-1975, mRNA Vaccine Candidates for Prevention of Lyme Disease in Healthy Adults: Interim Results of a Phase 1/2, Randomized, Observer-Blind, Placebo-Controlled, Dose-Ranging Trial

Nina Lin,* Doran Fink, Meredith Finn, Jacqueline Dooley, Rujun Teng, Emma Viscidi, Tin Bartholomew, Anthony Rizk, Christina Dold

Moderna, Inc., Cambridge, MA, USA

*Presenting author.

BACKGROUND

- Lyme disease, caused by infection with *Borrelia* bacteria, is a prevalent tick-borne illness that poses a substantial health burden due to its increasing incidence and potential to cause long-term morbidity, particularly in individuals with delayed diagnosis or inadequate treatment[1,2]
- A single *Borrelia* species, *B. burgdorferi*, is responsible for most infections in North America, whereas multiple *Borrelia* species cause infections in Europe[3]
- Previously developed Lyme disease vaccines targeting the *Borrelia* outer surface protein A (OspA) antigen were shown to elicit antibody responses that correlated with protection[4]; however, there are no Lyme disease vaccines currently approved for use in humans[5]
- Two investigational mRNA-based lipid nanoparticle vaccines encoding *Borrelia* OspA serotypes are in development
  - The monovalent vaccine mRNA-1982 contains mRNA encoding the *B. burgdorferi* serotype 1 (ST1) OspA antigen
  - The heptavalent vaccine mRNA-1975 encodes OspA serotypes that are expressed by the 4 major *Borrelia* species (ST1-7) that cause disease in North America and Europe

OBJECTIVE

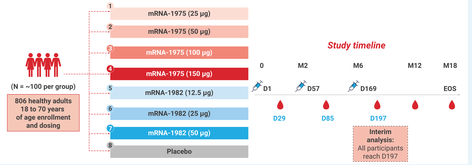
- To evaluate reactogenicity, safety, and immunogenicity of mRNA-1982 and mRNA-1975 against Lyme disease in healthy participants aged 18-70 years

METHODS

Trial Design and Participants

- This is an ongoing, randomized, observer-blind, placebo-controlled, phase 1/2 dose-ranging trial (NCT05975099) of mRNA-1982 (12.5, 25, or 50 µg) and mRNA-1975 (25, 50, 100, or 150 µg) administered as a 3-dose series at 0, 2, and 6 months in healthy adults aged 18-70 years (**Figure 1**)
- Interim findings through 7 months (1 month after the third injection) are presented herein

Figure 1. Study Design



D, day; EOS, end of study; M, month.

Trial Objectives and Endpoints

- The primary objective is to evaluate the safety and reactogenicity of mRNA-1982 and mRNA-1975
  - Endpoints include solicited local and systemic adverse reactions (ARs) and unsolicited adverse events (AEs) through 7 and 28 days after each trial injection, respectively; medically attended AEs (MAAEs) through 6 months after the last injection; and AEs of special interest (AESIs), serious AEs (SAEs), and AEs leading to discontinuation from injection and/or participation in the trial through the end of the study
- The secondary objective is to evaluate humoral immunogenicity elicited by mRNA-1982 and mRNA-1975
  - Endpoints include geometric mean concentration (GMC) and geometric mean fold rise (GMFR) of anti-OspA binding immunoglobulin G (IgG) antibodies at Days 1, 29, 85, and 197
- An exploratory objective is to evaluate antibody responses elicited by mRNA-1982 and mRNA-1975 equivalent to the LA-2 monoclonal antibody (mAb), a recombinant mAb that specifically binds to a key protective OspA epitope, with known bactericidal activity specifically against *Borrelia* ST1

RESULTS

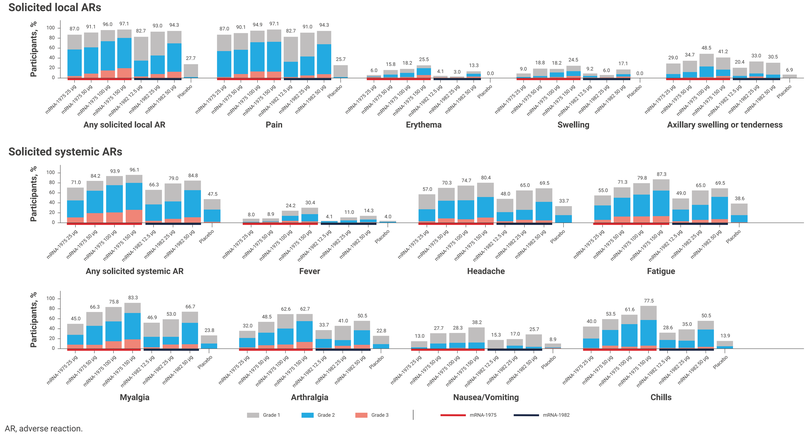
Participants

- At data cutoff (July 26, 2024), a total of 807 participants were randomized; 806 participants (99.9%) received the first injection, 777 (96.3%) received the second injection, and 745 (92.3%) received the third injection
  - Approximately 1% of enrolled participants were seropositive at baseline for prior *Borrelia* infection
- Across all study groups, the median age of participants was 52 years, with relatively equal distribution between males and females, and the majority were White (76.9%)

Reactogenicity and Safety

- The proportions of participants reporting any solicited local and systemic ARs generally increased in a dose-dependent manner across all dose levels in both mRNA-1982 and mRNA-1975 study groups (**Figure 2**)
- For both vaccines, solicited local and systemic ARs were generally highest after the third injection, but greater incremental increases were observed between the first and second injections
- The majority of the ARs were grade 1-2 in severity, and no grade 4 ARs were reported
  - Across all study groups, injection site pain, fatigue, headache, and myalgia were the most frequently reported solicited local and systemic ARs within 7 days after the first, second, and third injections
- There were no deaths and no related SAEs, AESIs, or AEs leading to discontinuation reported through the data cutoff

Figure 2. Solicited Local and Systemic ARs From Day 1 Through Day 7 After Any Study Injection



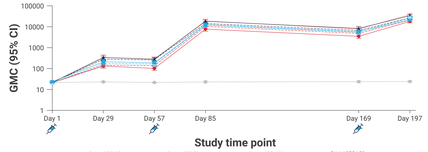
AR, adverse reaction.

Immunogenicity

1. Anti-OspA binding IgG

- Both vaccines elicited GMC anti-OspA binding IgG responses in a dose-dependent manner, with greater fold increase from baseline after each successive injection
  - At Days 29, 85, and 197, anti-OspA ST1 (**Figure 3**) and anti–OspA ST2-7–specific binding IgG GMFRs increased from baseline and were dose-dependent across all study groups
  - GMFRs declined by approximately 50% in the 3-month time frame between the second and third injections, with the highest GMFRs observed following the third injection in all study groups

Figure 3. GMC of Anti–OspA ST1 Binding IgG Antibodies (Per-Protocol Set)

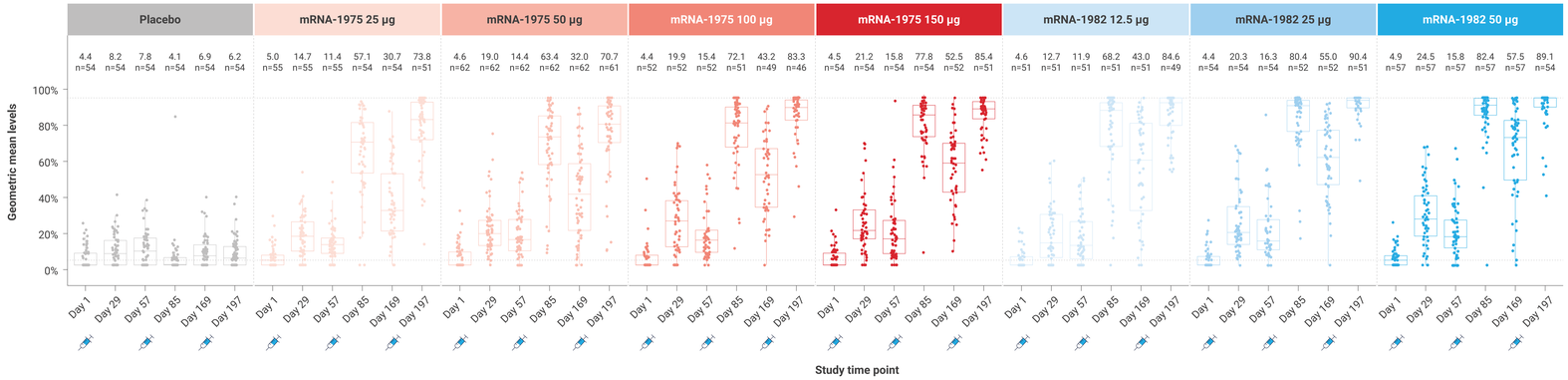


D, day; GMC, geometric mean concentration; IgG, immunoglobulin G; OspA, outer surface protein A; ST, serotype.

2. LA-2 inhibition

- Both mRNA-1982 and mRNA-1975 elicited antibodies that competed with the LA-2 mAb in a dose-dependent manner
- Levels of LA-2 inhibition increased with each successive injection, with modest increases after the third versus second injection (**Figure 4**)

Figure 4. Geometric Mean of LA-2 Inhibition (Per-Protocol Set)



CONCLUSIONS

- mRNA-1982 and mRNA-1975 were generally well-tolerated, with no safety concerns identified through data cutoff, by which time all participants had completed the 1-month post-third injection visit
- Both vaccines elicited dose-dependent reactogenicity and immunogenicity that increased with each successive injection
- LA-2 inhibition data indicate that both the mRNA vaccines encode a structurally accurate OspA ST1, which elicits antibodies targeting a key bactericidal epitope known to confer protection
- Complementary serum bactericidal activity assessments measuring the net bactericidal activity of all serotype epitopes are underway across multiple time points for both compositions
- These data will inform the vaccines, regimens and dose ranges to be evaluated in future clinical trials

ADDITIONAL INFORMATION

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For additional information, please contact Nina Lin (nina.lin@modernatx.com).

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Disclosures

NL, MF, JD, RT, EV, TB, AR, and CD are employees of Moderna, Inc., and may hold stock/stock options in the company.