Program Pack

CMV (mRNA-1647)

Cytomegalovirus (CMV) Overview

CMV is the most common infectious cause of birth defects in the U.S.[1] and is responsible for several billion dollars in annual healthcare costs[2]

Sequelae include

At birth:

- Microcephaly
- Chorioretinitis
- Seizures
- Sensorineural hearing loss

1 in 200

babies in the U.S. are born with a congenital CMV infection (CMV infection is present at birth)

Long term:

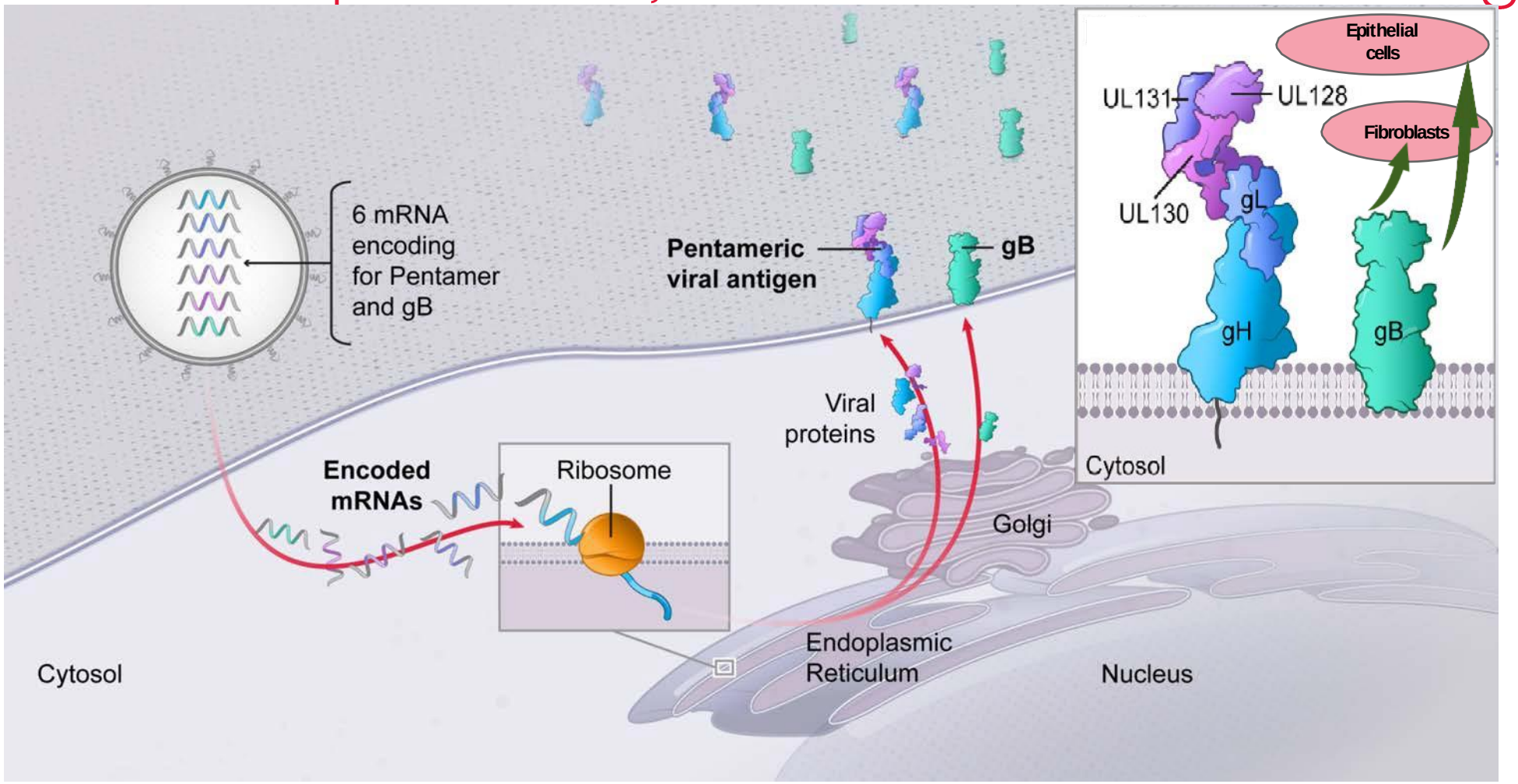
- Cognitive impairment
- Cerebral palsy
- Seizure disorder
- Sensorineural hearing loss

1 in 5

will have severe, life-altering health problems

1. CDC, https://www.cdc.gov/cmv/congenital-infection.html; 2. Grosse, Scott et al. "Economic assessments of the burden of congenital cytomegalovirus infection and the cost-effectiveness of prevention strategies," *Seminars in perinatology,* 2021, https://doi.org/10.1016/j.semperi.2021.151393

Our CMV vaccine (mRNA-1647) includes 6 mRNAs (five encode the pentamer, the 6th encodes for the gB antigen)



CMV vaccine (mRNA-1647) Phase 3 trial accruing cases with final analysis expected in 2025

Randomized, observer-blind, placebo-controlled study to evaluate the **efficacy, safety and immunogenicity of mRNA-1647 to evaluate prevention of primary infection**

Enrollment complete in the U.S. and internationally across 290 sites globally

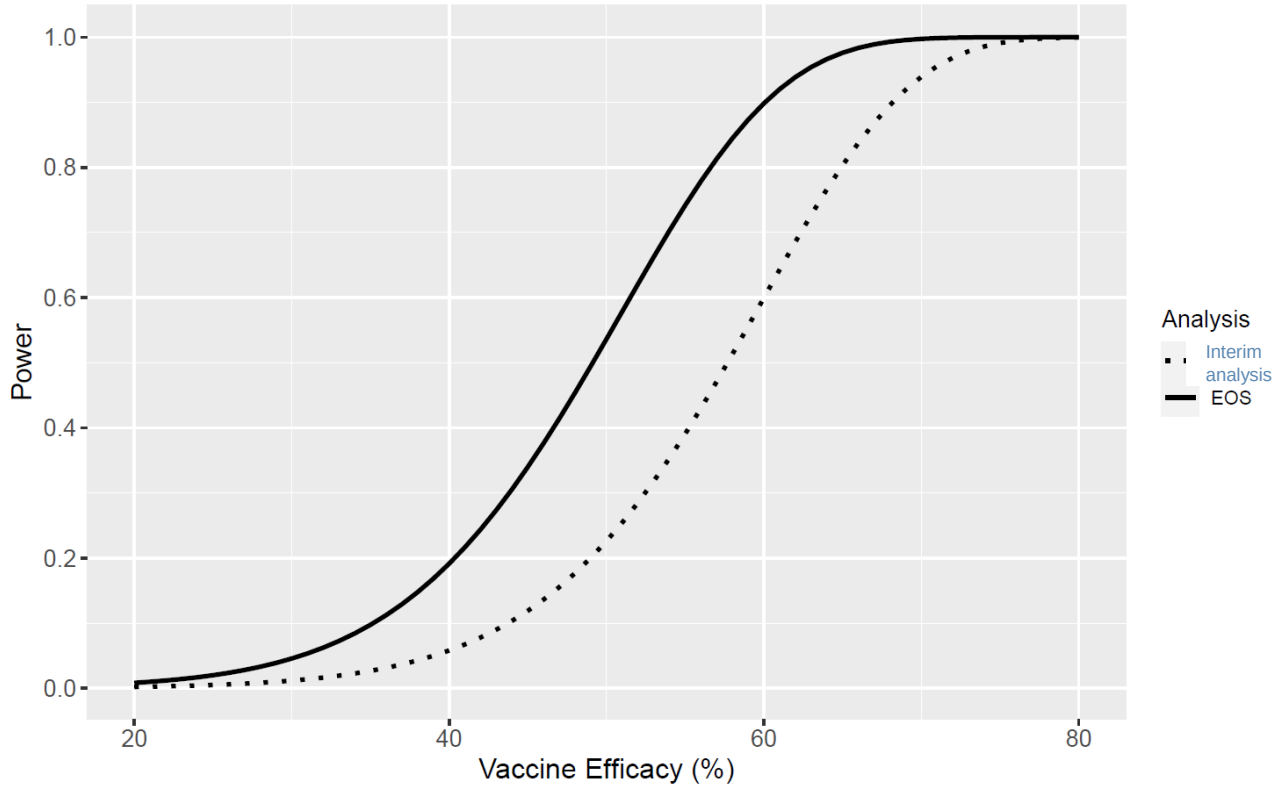
Participants older than 20 years of age were enrolled only if they had contact with young children

The Data Safety Monitoring Board (DSMB) met to review the initial study data. The criterion for early efficacy was not met. The Company remains blinded and anticipates final efficacy data from the study in 2025

Overview of primary efficacy endpoint

Efficacy Boundaries with Alpha-allocation between 2 Planned Analyses

	Approximate # of Cases	One-sided Alpha	VE: Efficacy Bound
Interim Analysis (did not meet)	81	0.5%	~ 57.7%
End of Study (EOS) Analysis	112	2.0%	~ 49.1%



CMV (mRNA-1647) Phase 3 vaccine summary and next steps

Addressing disease burden

- CMV is the most common cause of congenital infection worldwide[1]
- Moderna's CMV vaccine targets two antigens, the pentamer and the glycoprotein B (gB) antigen

Latest updates

- CMV Phase 3 trial is accruing cases

Next steps

- Expect final analysis in 2025

Sources: (1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8453618/

CMV vaccine (mRNA-1647) Phase 1 data summary (12-month IA)

Generally well-tolerated, no vaccine-related serious adverse events (SAEs)

Neutralizing antibody (nAb) response, CMV-seronegative group

At 1 month after the 3rd vaccination, nAb geometric mean titers (GMTs) against epithelial cell infection (measuring pentamer response) ranged 2.8-fold to 17-fold higher than the CMV-seropositive baseline GMT benchmark, and nAb GMTs against fibroblast infection (measuring gB response) ranged 0.8-fold to 5.0-fold higher than the CMV-seropositive baseline GMT benchmark

Neutralizing antibody titers in the CMV-positive group

At 1 month after the 3rd vaccination, the ratio of nAb titers compared to baseline (geometric mean ratios, or GMRs) against epithelial cell infection ranged 13.4-40.8 and against fibroblast infection ranged 4.0-7.1

Early evidence of immune persistence out to 12 months (6 months after the 3rd vaccination)

Key changes to mRNA-1647 in Phase 2 clinical trial

Improved Potency

- Improved ratio of mRNA components to increase potency

Improved Tolerability

- Optimized the manufacturing process to improve tolerability

Lyophilization

- Phase 2 utilizes the intended Phase 3 and commercial formulation

Liquid, Single-Dose Vial,
-20°C storage ≥6 months shelf-life

Lyophilized, Single-Dose (0.5mL),
5°C storage ≥ 18months shelf-life

CMV vaccine (mRNA-1647) Phase 2 trial overview

Key objective

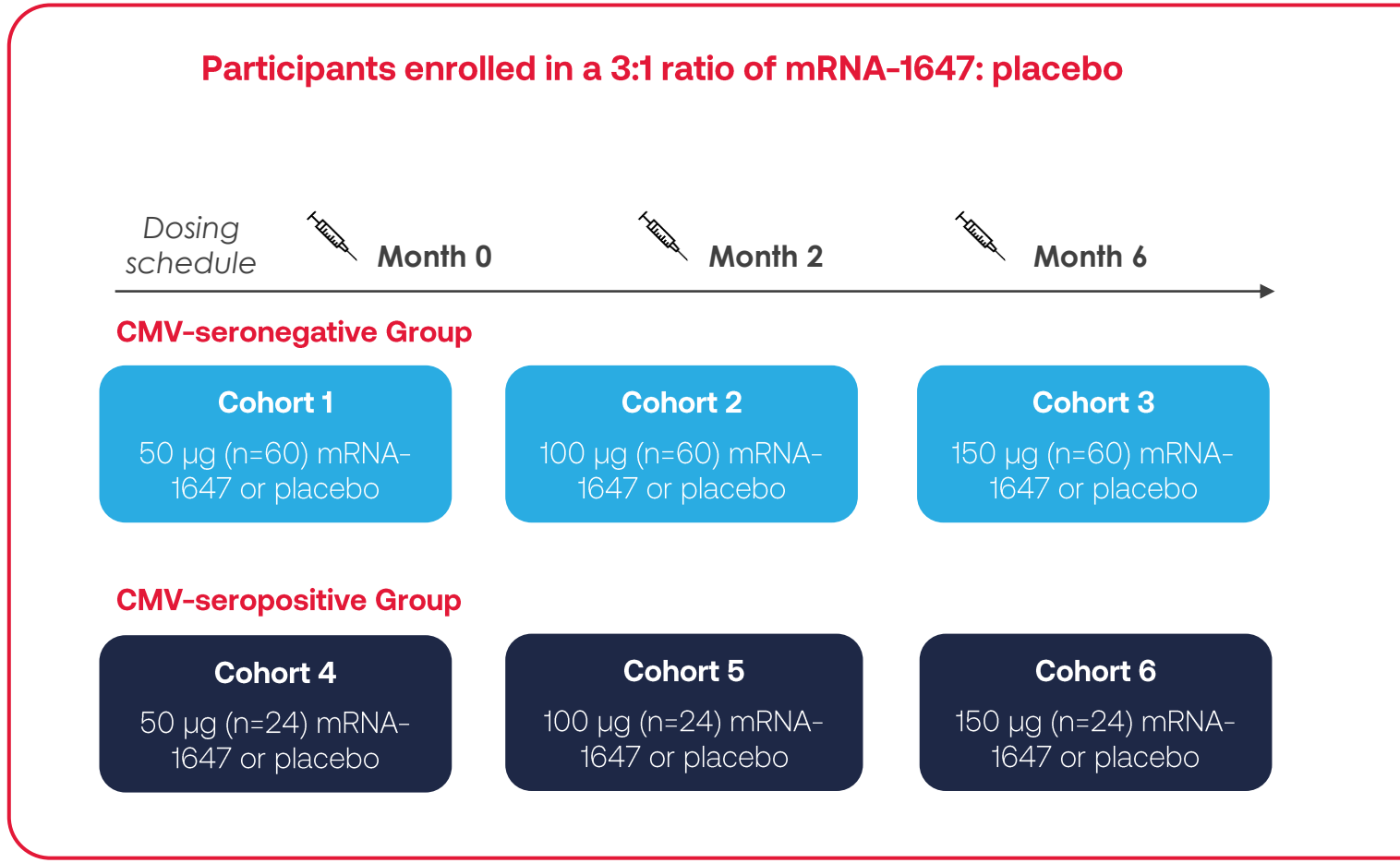
- To assess the safety and immunogenicity of mRNA-1647 vaccine in its Phase 3 presentation to select a dose level to progress into Phase 3 development

Primary endpoints

- Defined safety parameters
- Pentamer-specific and gB-specific neutralizing antibody responses as measured by epithelial cell and fibroblast assays

Secondary endpoints

- Pentamer-specific and gB-specific binding IgG responses as measured by ELISA



Phase 2 Study of mRNA-1647 in Healthy Adults (NCT04232280)

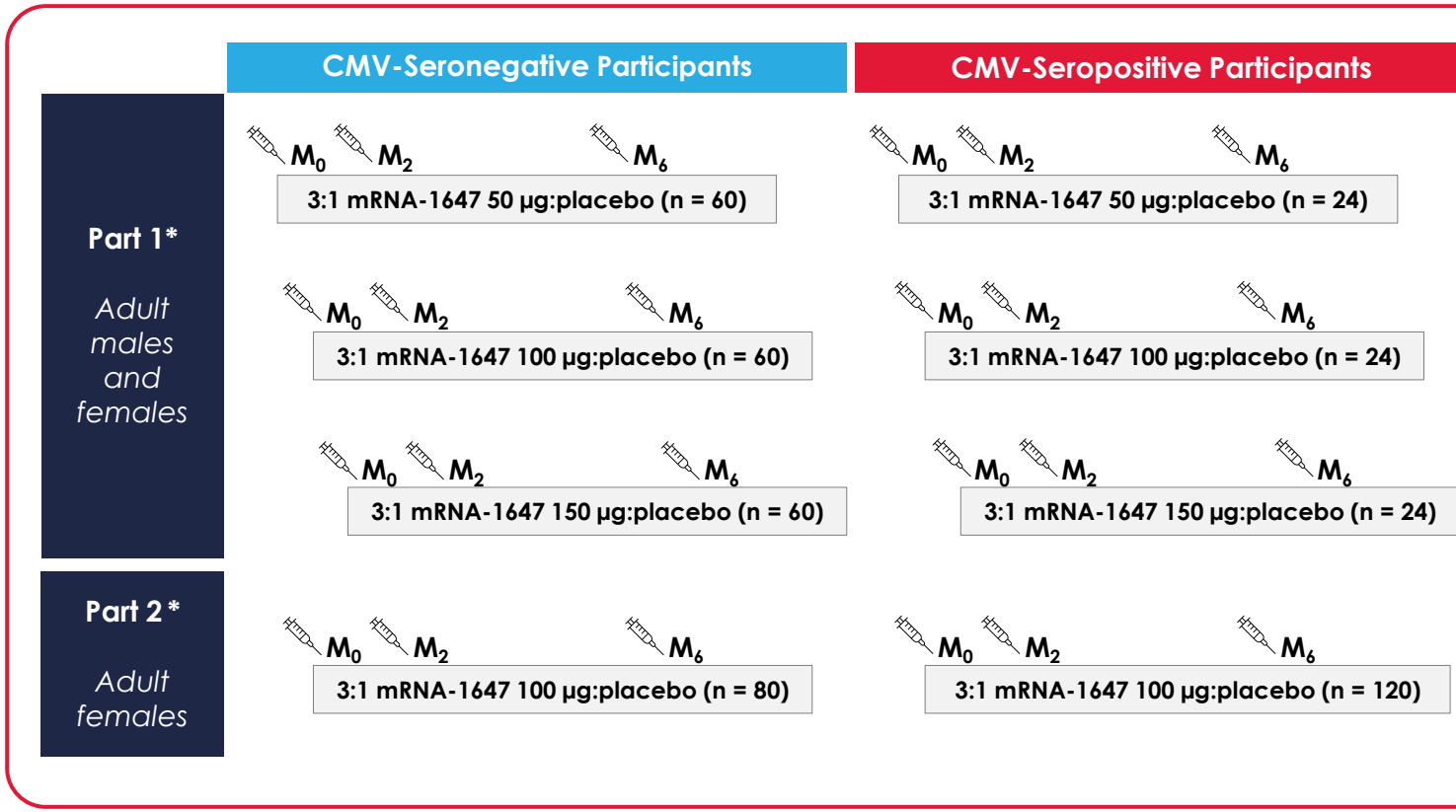
This phase 2, randomized, placebo-controlled, observer-blind, dose-finding trial evaluated the safety and immunogenicity of mRNA-1647 in healthy CMV-seronegative and CMV-seropositive US adults aged 18-40 years

Safety Endpoints

- Solicited local and systemic ARs through 7 days after each dose
- Unsolicited AEs within 28 days after each dose
- MAAEs 6 months after each dose
- SAEs throughout the entire study period

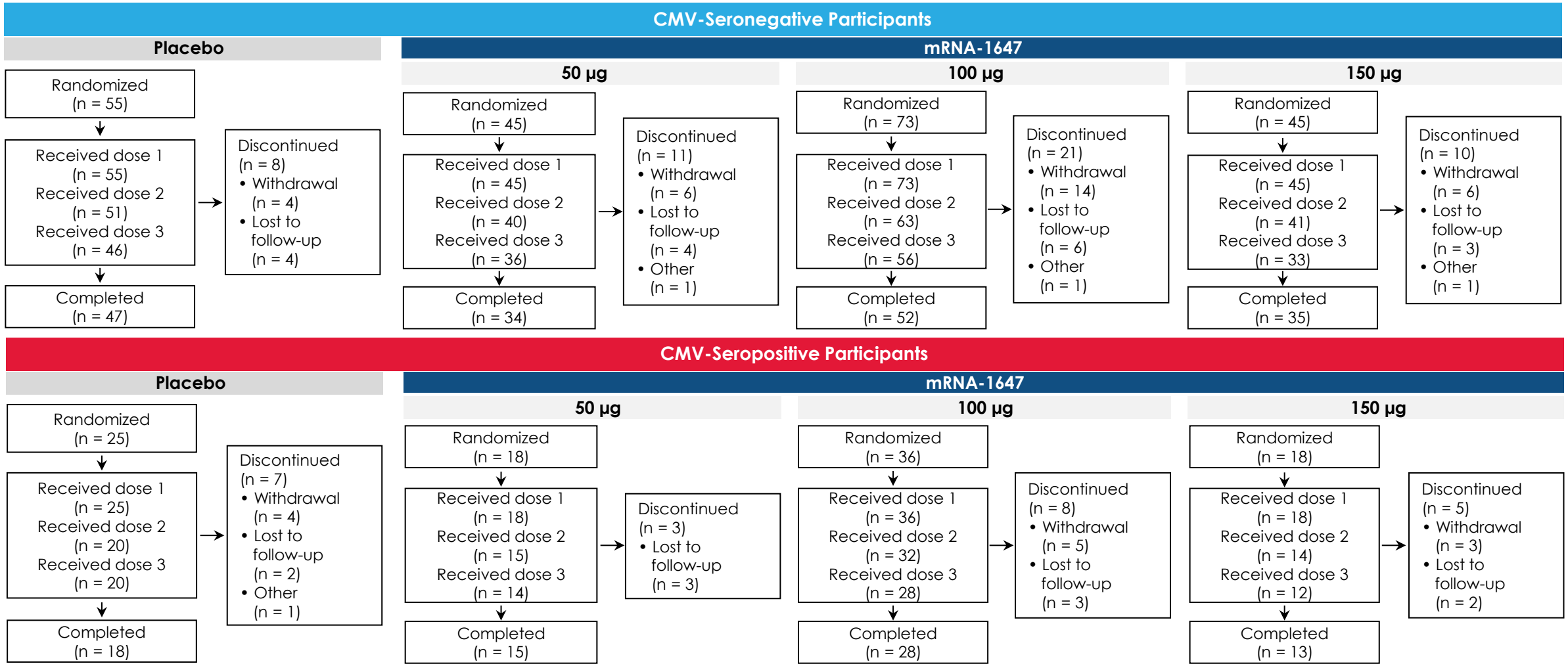
Immunogenicity Endpoints

- nAb titers on D1, 29, 56, 84, 168, 196, 336, and 504 against:
  - Epithelial cell infection (a measure of functional antibody response to pentamer antigen)
  - Fibroblast infection (a measure of functional antibody response to gB antigen)
- Anti-gB and anti-pentamer binding IgG D1, 29, 56, 84, 168, 196, 336, and 504
- gB- and pentamer-specific T-cell responses on D1 and 8, M2, D63, M6, D175, and M12 and 18



*Data from Parts 1 and 2 were combined.
AE, adverse event; AR, adverse reaction; CMV, cytomegalovirus; D, day; gB, glycoprotein B; IgG, immunoglobulin G; M, month; MAAE, medically attended AE; nAb, neutralizing antibody; SAE, serious AE.

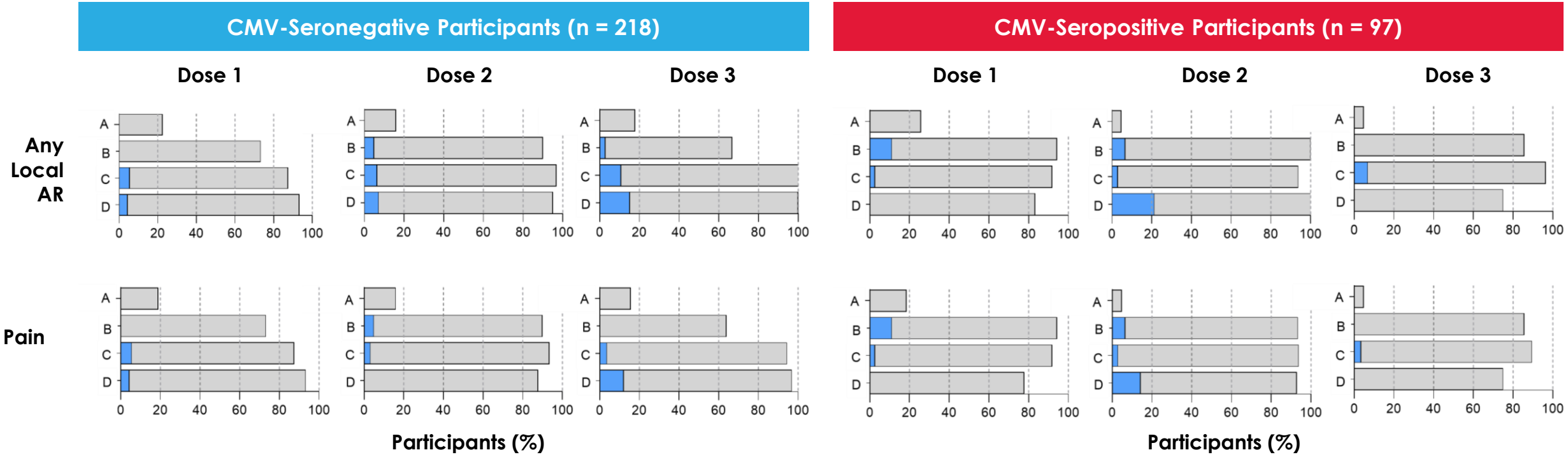
Participant Disposition



- A total of **315 participants were randomized** (252 participants in Part 1 [109 male and 143 female] and 63 participants in Part 2 [all female])
- Overall, **242** (76.8%) **participants completed the trial**

Study c

Most Common Solicited Local Adverse Reactions by CMV Serostatus

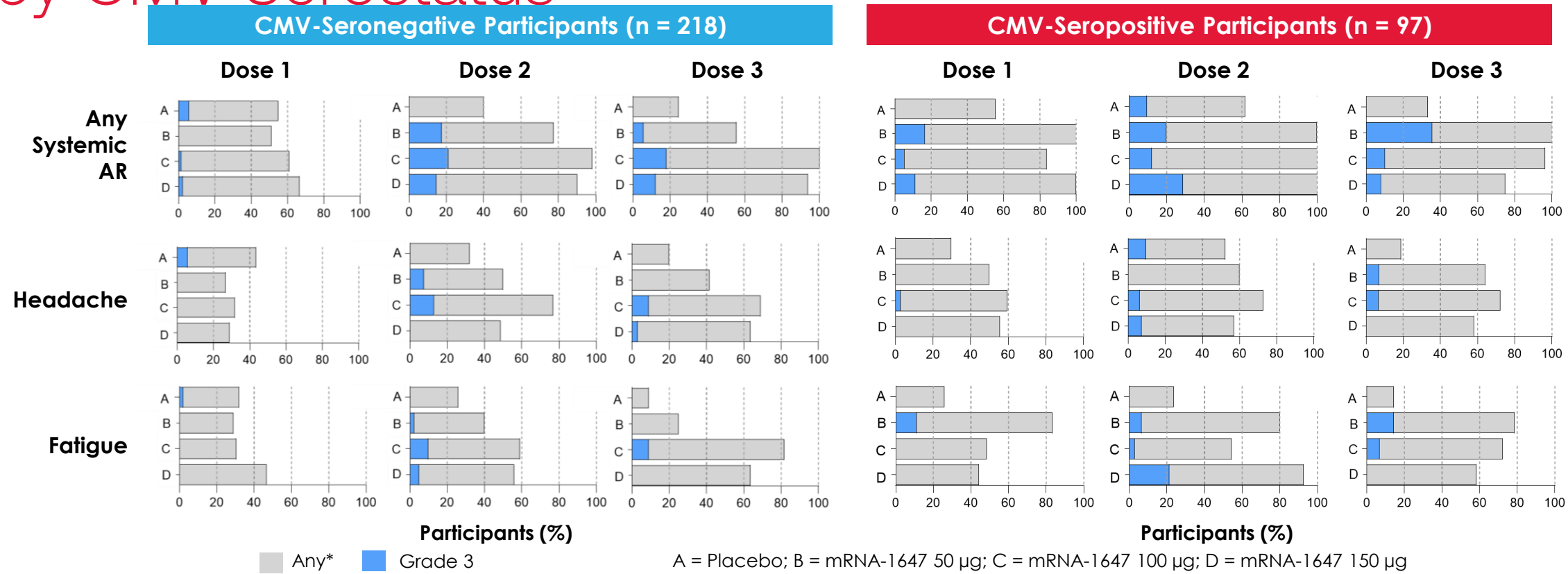


A = Placebo; B = mRNA-1647 50 µg; C = mRNA-1647 100 µg; D = mRNA-1647 150 µg

- Most local ARs after mRNA-1647 vaccination were grade 1 or 2 in severity; no grade 4 local ARs were reported
  - Injection site pain was the most frequently reported
  - There were no differences in incidence between serostatus groups

*Any includes grades 1, 2, and 3.
AR, adverse reaction; CMV, cytomegalovirus.

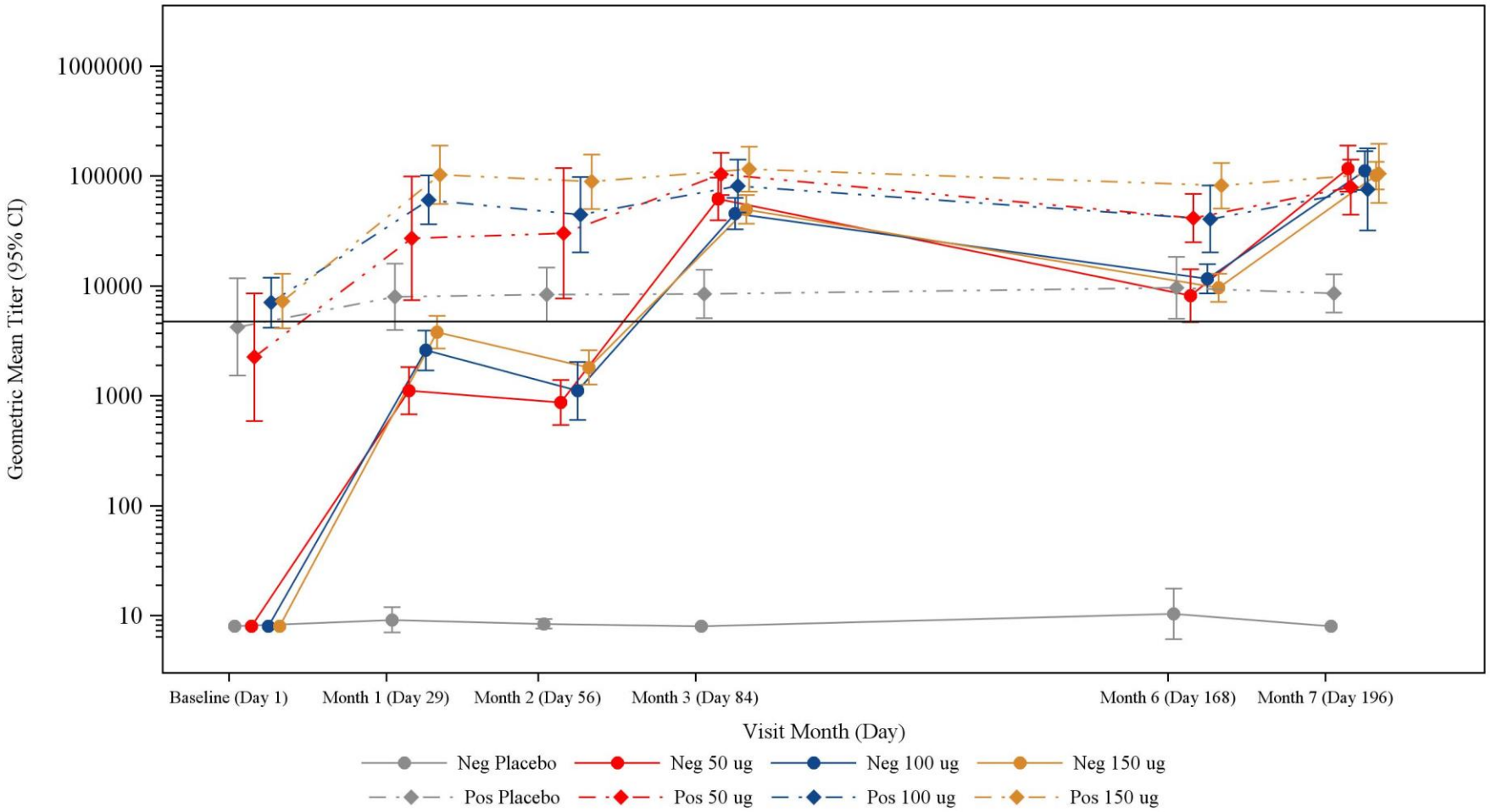
Most Common Solicited Systemic Adverse Reactions by CMV Serostatus



- Most systemic ARs after mRNA-1647 vaccination were grade 1 or grade 2 in severity; fever was the only grade 4 systemic AR reported (1.3% and 2.0% after doses 1 and 2, respectively; 1.3% after placebo)
  - Headache and fatigue were the most frequently reported
  - Incidence of any systemic AR was generally higher for CMV-seropositive than for CMV-seronegative participants

*Any includes grades 1, 2, and 3.
AR, adverse reaction; CMV, cytomegalovirus.

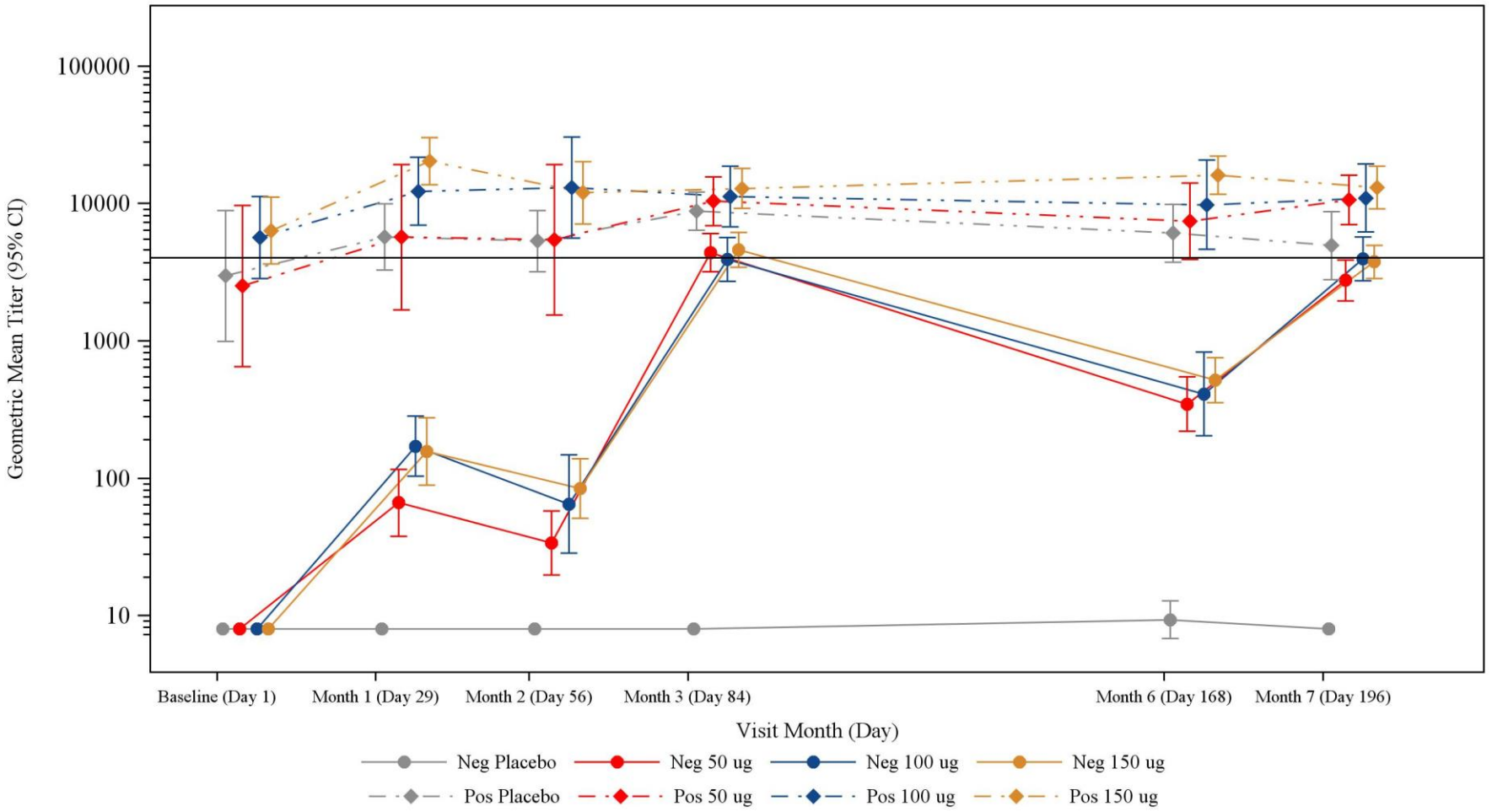
Neutralizing antibody titers against epithelial cell infection through Month 7



Neutralizing antibodies against epithelial cell infection:

- Increased in a dose-related manner after the 1st vaccination in both seronegative and seropositive participants
- Increased further after the 2nd vaccination and again after the 3rd vaccination to GMTs exceeding the seropositive benchmark GMTs in all treatment groups by over 20-fold

Neutralizing antibody titers against fibroblast cell infection through Month 7

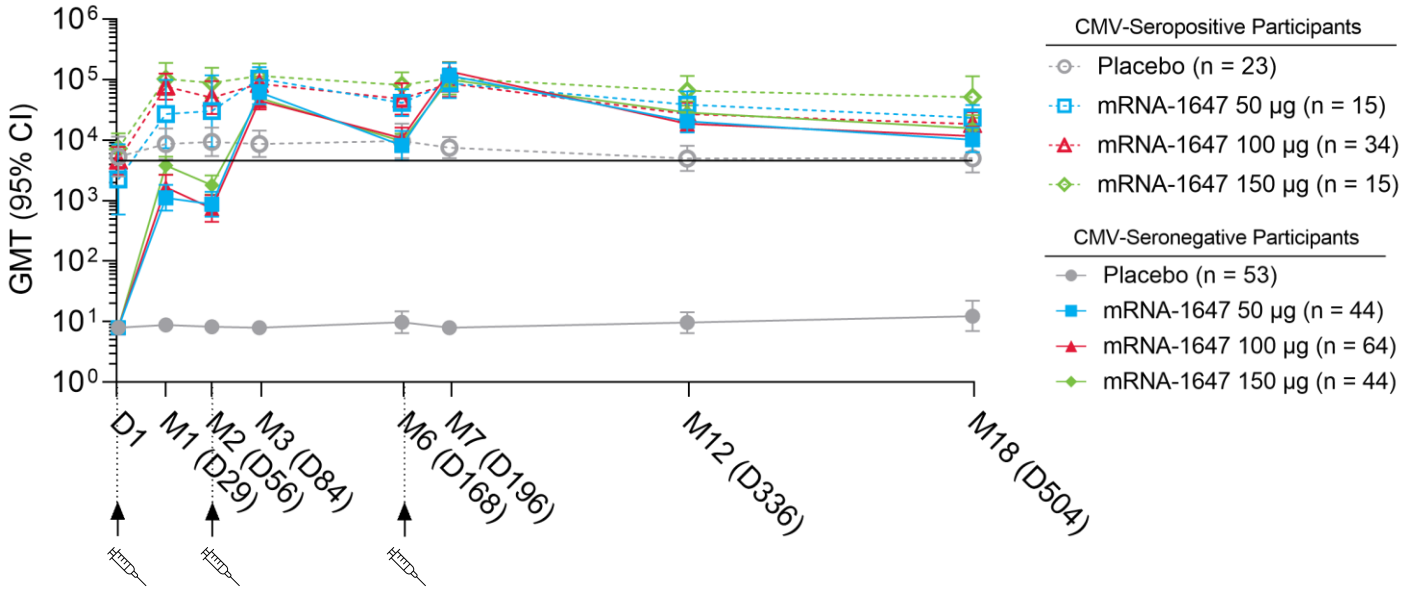


Neutralizing antibodies against fibroblast infection:

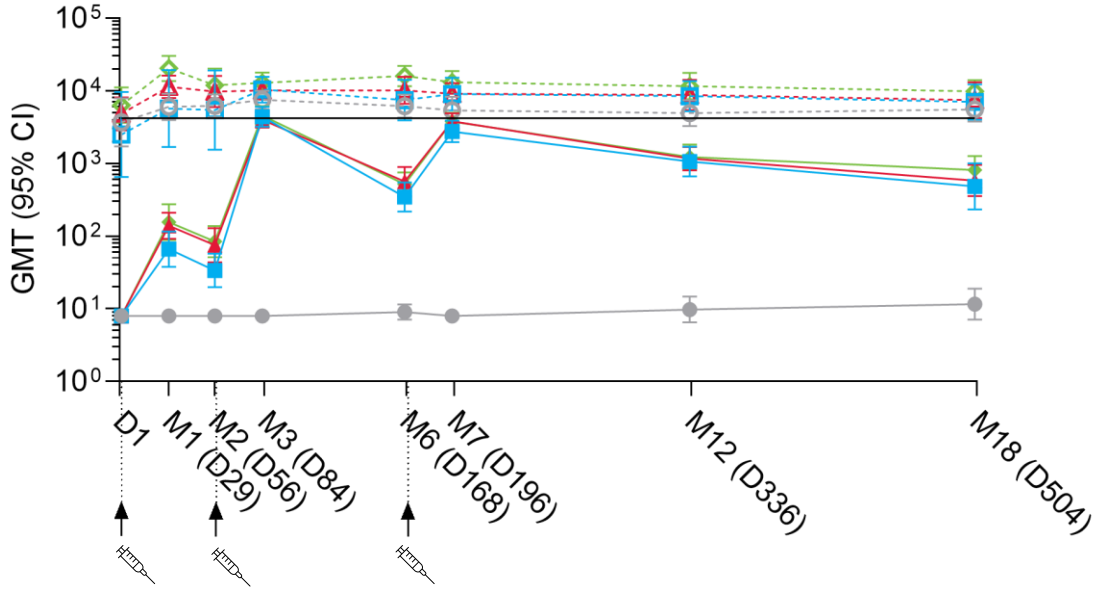
- Increased after the 2nd vaccination to GMTs approaching or exceeding the seropositive benchmark GMT in all treatment groups
- After the 3rd vaccination, GMTs in the 100 µg and 150 µg treatment groups were comparable to GMTs after the 2nd vaccination

Antibody-Mediated Immunogenicity by CMV Serostatus: Neutralizing Antibodies

nAbs Against Epithelial Cell Infection



nAbs Against Fibroblast Infection



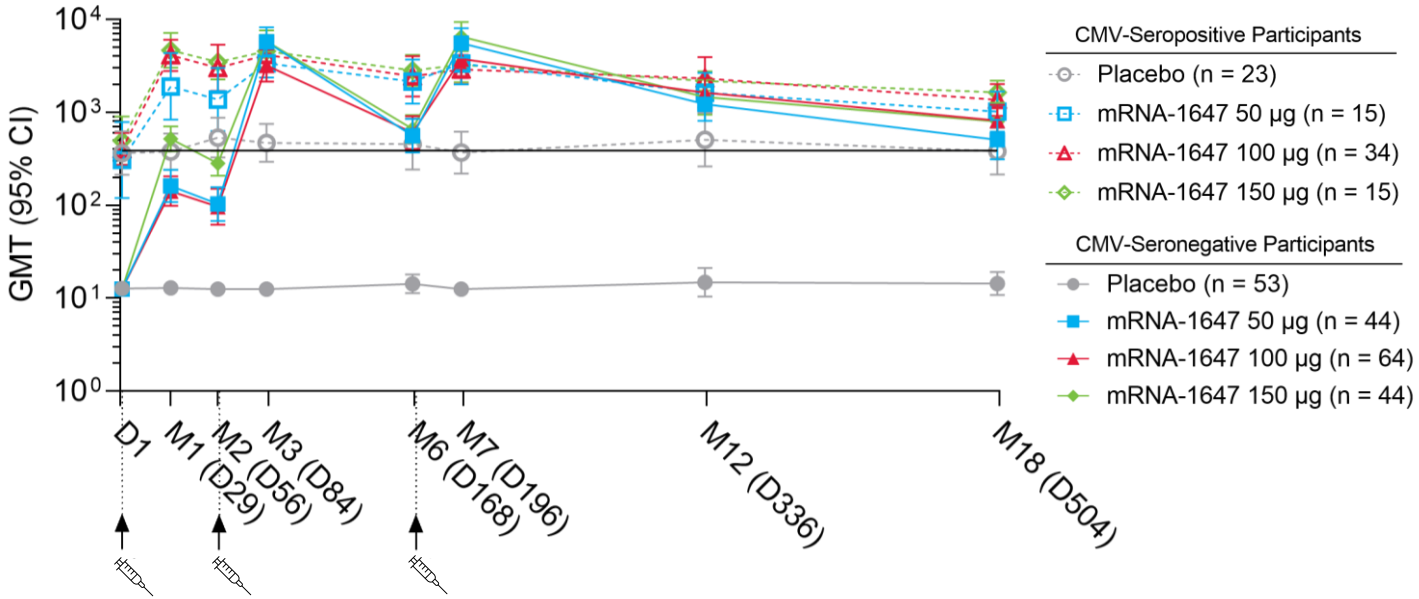
- ***CMV-seronegative:*** nAbs against epithelial cell infection increased after mRNA-1647 doses 1, 2, and 3
  - nAbs exceeded the CMV-seropositive benchmark after doses 2 and 3 and remained above the benchmark through M18
- ***CMV-seropositive:*** nAbs against epithelial cell infection increased after after mRNA-1647 dose 1
  - nAbs after doses 2 and 3 were comparable to or exceeded those after dose 1

- ***CMV-seronegative:*** nAbs against fibroblast infection increased after mRNA-1647 doses 1, 2, and 3
  - nAbs approached or exceeded the CMV-seropositive benchmark
- ***CMV-seropositive:*** nAbs against fibroblast infection increased after mRNA-1647 dose 1
  - nAbs after doses 2 and 3 were generally similar to or higher than those after dose 1

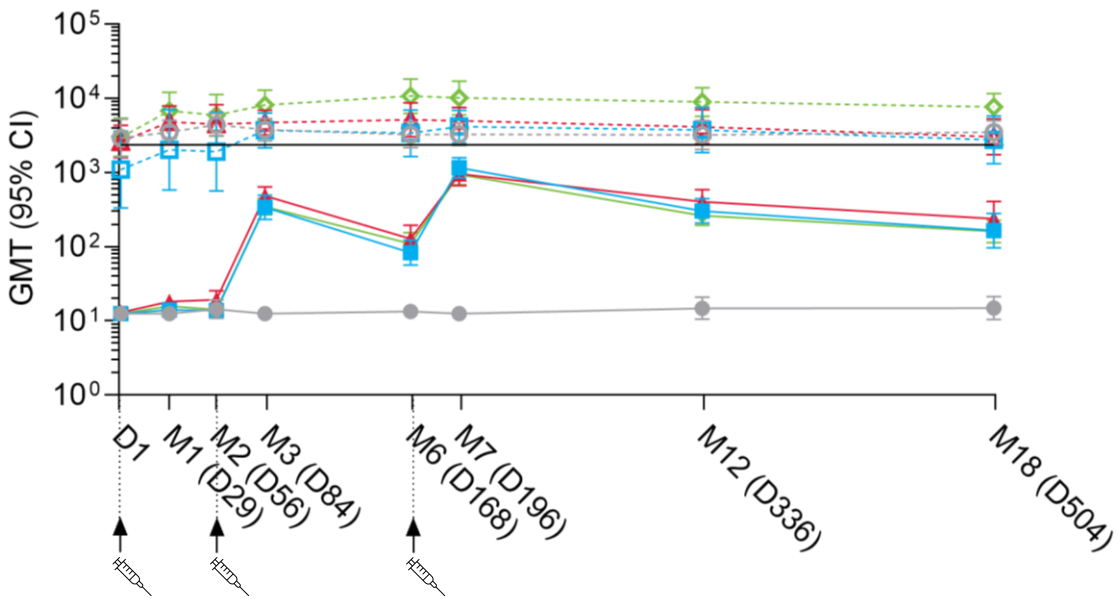
CMV, cytomegalovirus; D, Day; GMT, geometric mean titer; M, month; nAb, neutralizing antibody.

Antibody-Mediated Immunogenicity by CMV Serostatus: Binding Antibodies

Anti-Pentamer bAbs



Anti-gB bAbs



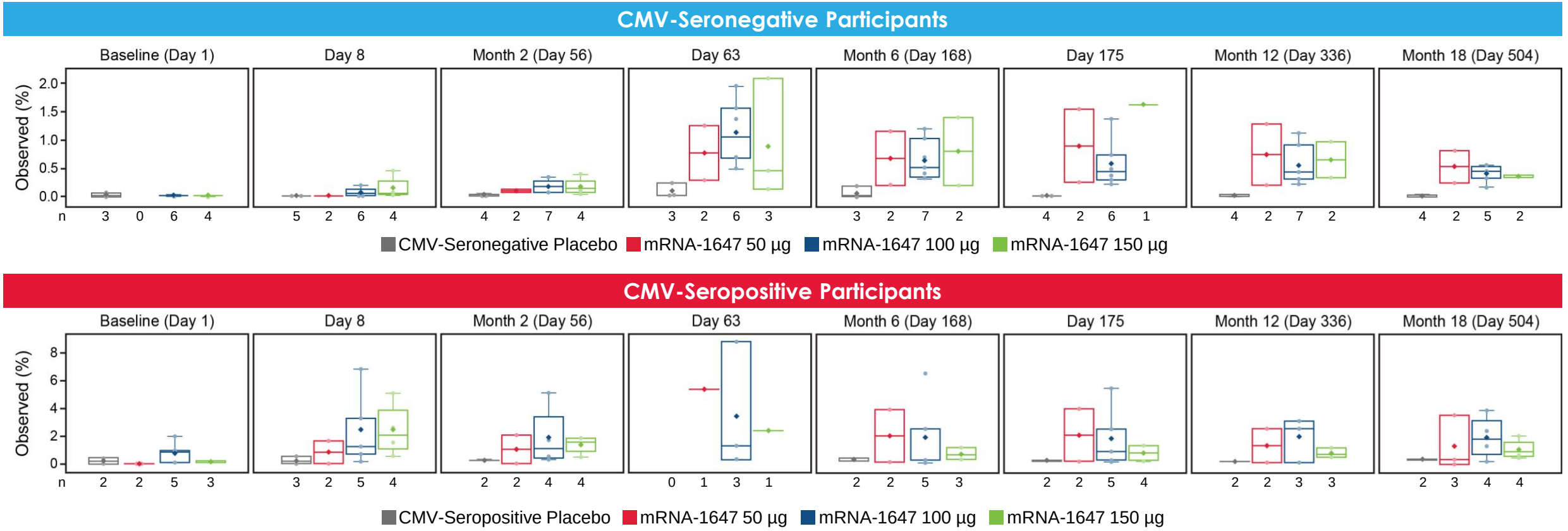
- ***CMV-seronegative:*** anti-pentamer bAbs increased after mRNA-1647 dose 1
  - bAbs exceeded the CMV-seropositive benchmark after doses 2 and 3 and remained above the benchmark through M18
- ***CMV-seropositive:*** anti-pentamer bAbs increased after mRNA-1647 dose 1
  - bAbs after doses 2 and 3 were comparable to those after dose 1

- ***CMV-seronegative:*** anti-gB bAbs increased after mRNA-1647 dose 2 and increased further after dose 3 but remained below the CMV-seropositive benchmark
- ***CMV-seropositive:*** anti-gB bAbs increased after mRNA-1647 dose 1
  - bAbs increased after doses 2 and 3 in the 50 µg and 150 µg groups

bAbs, binding antibodies; CMV, cytomegalovirus; D, Day; gB, glycoprotein B; GMT, geometric mean titer; M, month; nAb, neutralizing antibody.

Cell-Mediated Immunogenicity by CMV Serostatus

Non-Naive CD4+ Th1 Cells - gB (%)



- Antigen-specific CD4 T-cell responses were observed among mRNA-1647 dose groups in CMV-seropositive and CMV-seronegative participants compared with placebo recipients; responses peaked 1 week after dose 2 (Day 63)
- T-cell responses were detected against 3 CMV peptide pools (gB, gL/UL, gH) through Day 504

CMV, cytomegalovirus.

Phase 2 seven-month interim analysis conclusion

mRNA-1647 CMV vaccine was generally well tolerated

- The most common solicited local AR was injection site pain
- The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills
- In general, solicited AR frequency and severity after the 3rd vaccination were similar to or lower compared to the 2nd vaccination

In CMV-seronegative participants in mRNA-1647 treatment groups after the 3rd vaccination:

- Neutralizing antibody (nAb) GMTs against epithelial cell infection were at least 20-fold higher than the CMV-seropositive baseline GMT benchmark
- nAb GMTs against fibroblast infection approximated the CMV-seropositive baseline GMT benchmark

In CMV positive participants in mRNA-1647 treatment groups after the 3rd vaccination:

- nAb GMRs against epithelial cell infection increased to at least 6.8-fold over baseline
- nAb GMRs against fibroblast infection increased to approximately 2-fold over baseline

Phase 2 eighteen-month interim analysis conclusion

This analysis presents the safety and immunogenicity findings from the phase 2 clinical trial of mRNA-1647 in CMV-seronegative and CMV-seropositive healthy adults 18-40 years of age

mRNA-1647 was generally well-tolerated at all dose levels assessed (50 µg, 100 µg,150 µg) regardless of baseline CMV serostatus

There were no notable dose-related trends identified in solicited ARs or in unsolicited AEs

Among CMV-seronegative participants, nAbs against epithelial cell infection and against fibroblast infection increased after doses 1, 2, and 3 of mRNA-1647; nAbs against epithelial cell infection were above the CMV-seropositive benchmark through the end of the trial

Among CMV-seropositive participants, nAbs against epithelial cell infection and against fibroblast infection increased after dose 1 of mRNA-1647 only

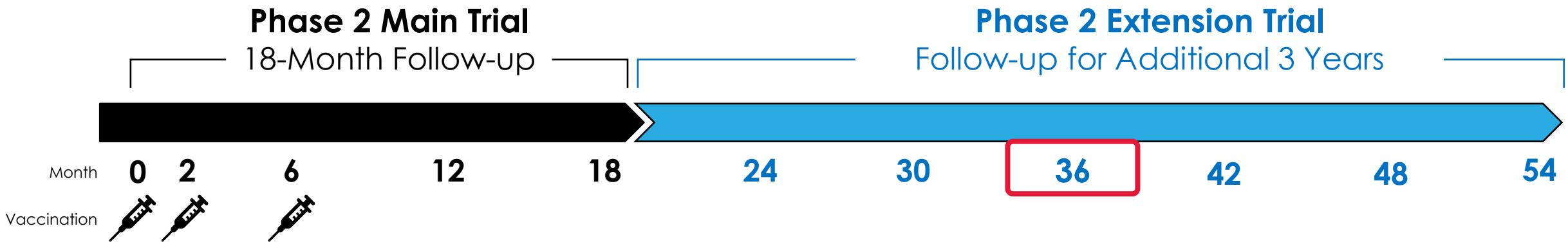
bAb responses generally aligned with the nAb findings

T-cell responses following mRNA-1647 were maintained through Day 504

Results from this study supported selection of the mRNA-1647 100-µg dose level for the ongoing phase 3 trial

Phase 2 Extension Trial in Adults to Assess Persistence of Antibody

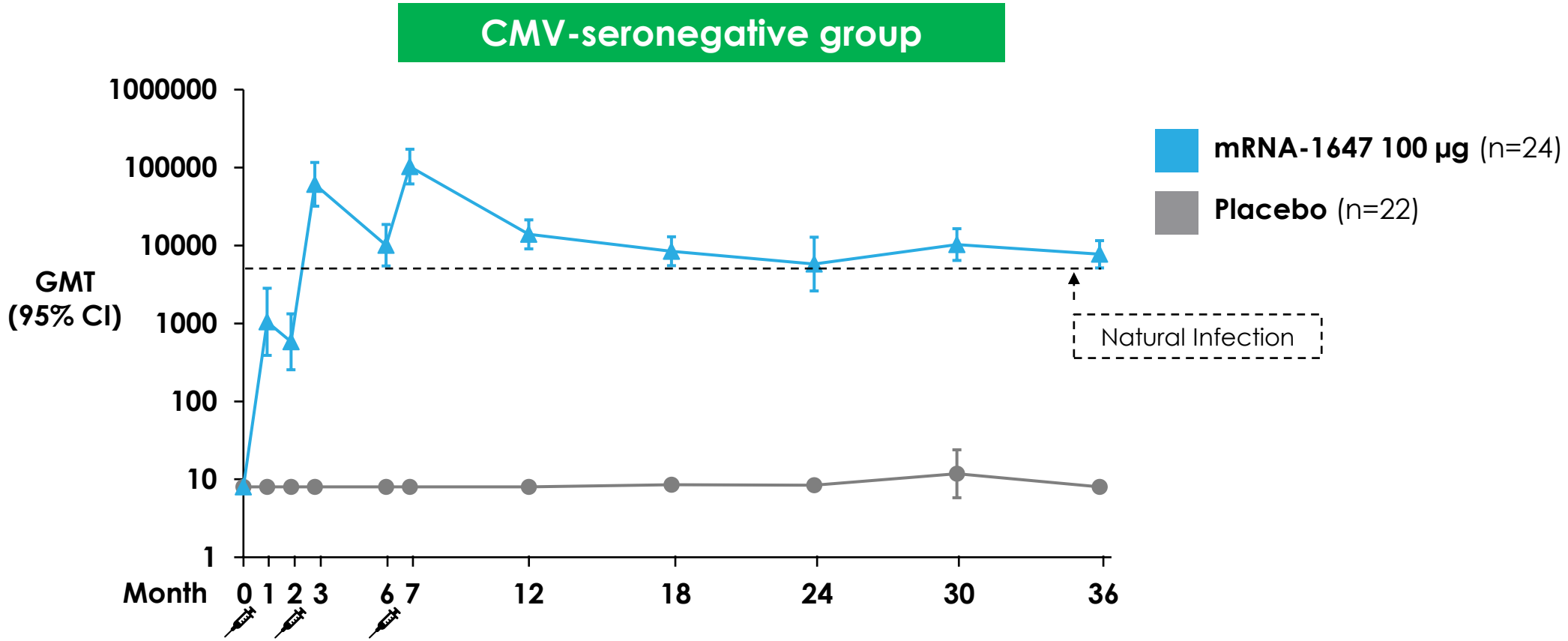
Design	• 3-year long-term follow-up of immunogenicity and safety in participants who completed the phase 2 original study • Provides ~4 years total follow-up after last vaccine dose
Objectives	• **Primary:** Safety and neutralizing antibody-mediated immunogenicity • **Secondary:** Binding antibody-mediated immunogenicity



ESCMID, 2025

Persistence **of Neutralizing Antibodies Against Epithelial Cell Infection** Demonstrated Through 3 Years After Vaccination

Interim analysis of participants followed for 36 months

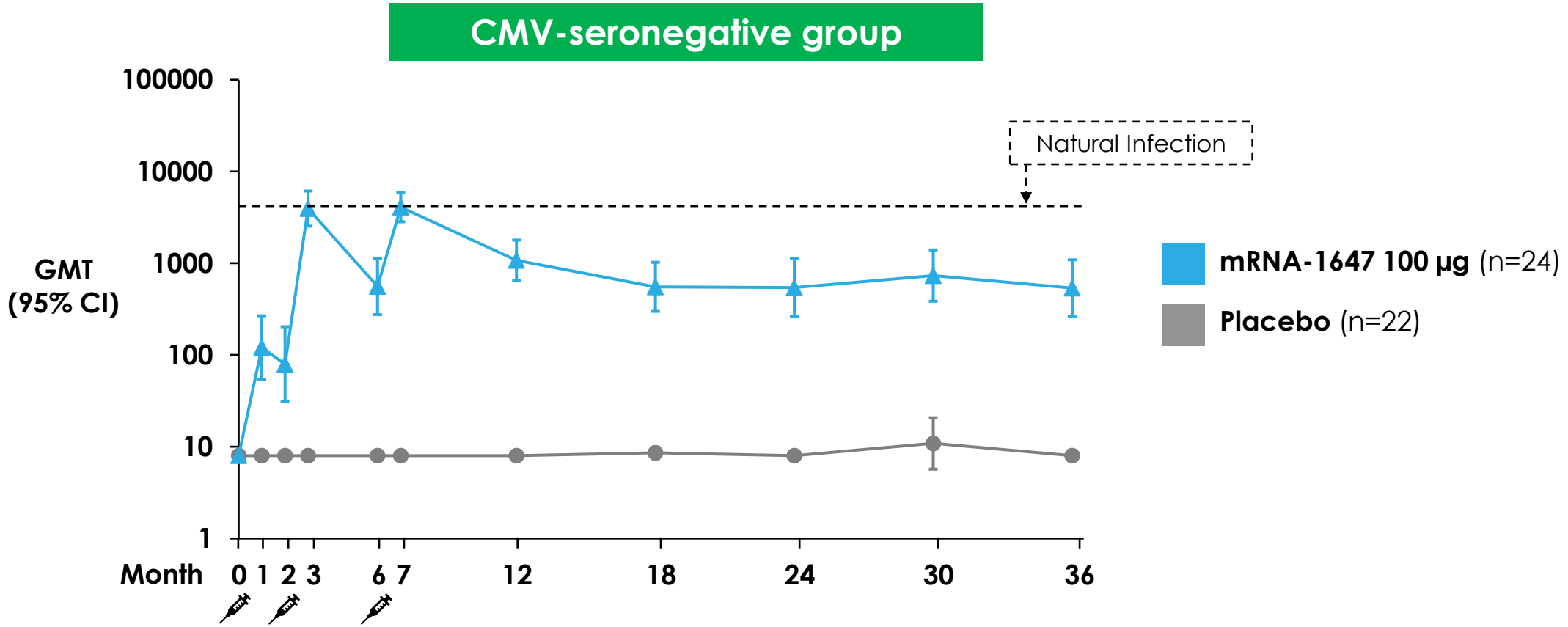


- Antibody GMTs remained stable
- nAb GMTs in CMV-seronegatives continued to exceed natural infection GMT through 3 years

ESCMID, 2025; GMT – geometric mean titer

Persistence of Neutralizing Antibodies Against Fibroblast Infection Demonstrated Through 3 Years After Vaccination

Interim analysis of participants followed for 36 months



- Antibody GMTs remained stable through 3 years

ESCMID, 2025; GMT – geometric mean titer

Summary: mRNA-1647 Phase 2 Trial in Adults (18-40 Years)

Safety	• Generally well tolerated; no safety concerns identified • 3-dose 100 µg regimen regardless of serostatus
Immunogenicity	• Highly immunogenic at 100 µg dose level • Neutralizing antibody GMTs against epithelial cell infection remained above natural infection GMT through 12 months after the last vaccination in CMV-seronegative participants • Boosting effect observed in CMV-seropositive participants
Persistence of Antibody	• Persistence of neutralizing antibodies against epithelial cell infection demonstrated through 3 years after vaccination in CMV-seronegative & seropositive participants

NCT05085366

CMV vaccine (mRNA-1647) indication expansion studies

Adolescents

(9-15 years old)

Phase 1/2 trial has begun enrollment

Transplant

(Adults)

Trial initiated

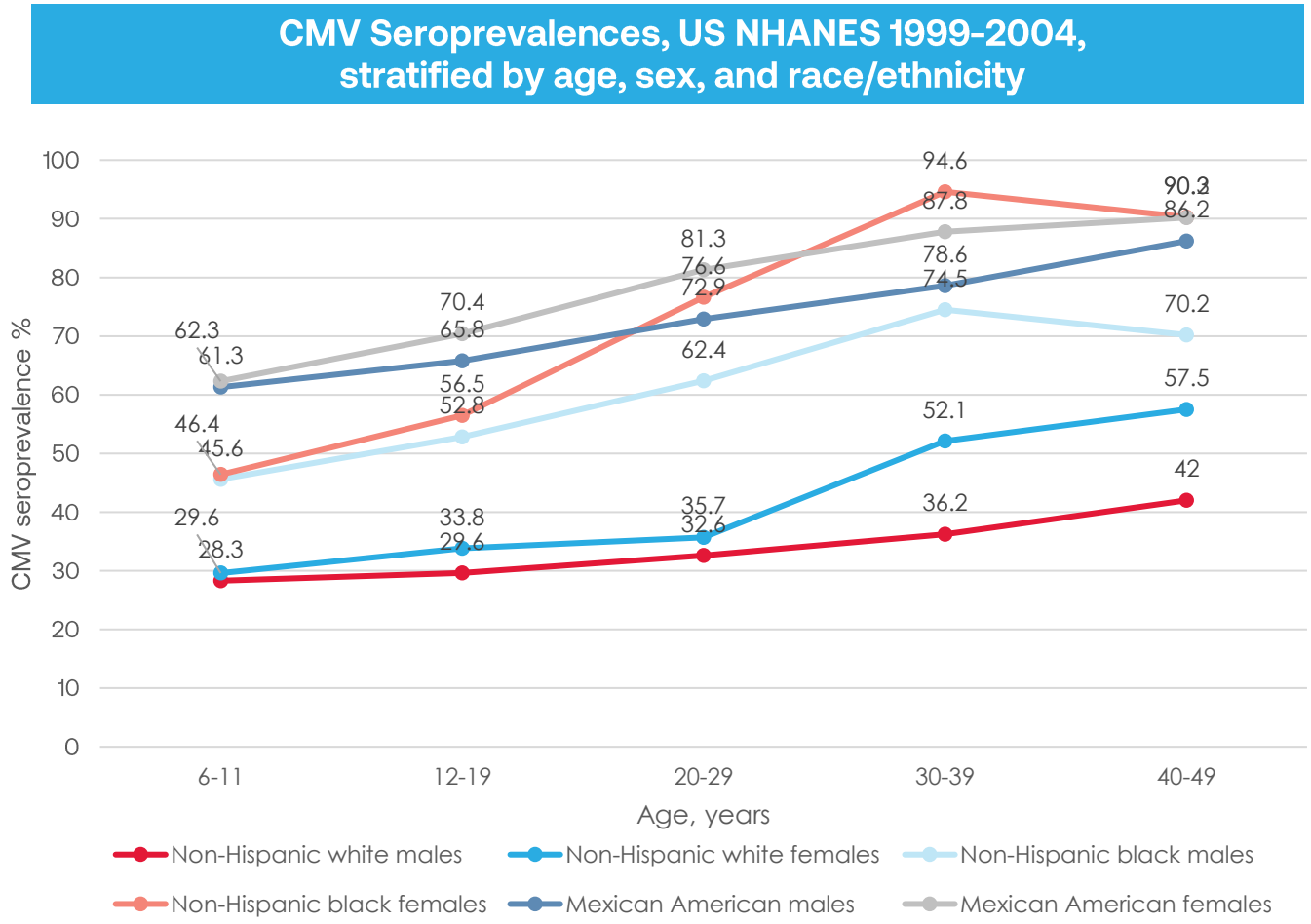
Ongoing enrollment

Sources: (1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8453618/

CMV vaccination in adolescents is aimed at primary prevention

- Because infection rates increase with age, **we will prevent a greater number of primary infections if we can vaccinate adolescents**

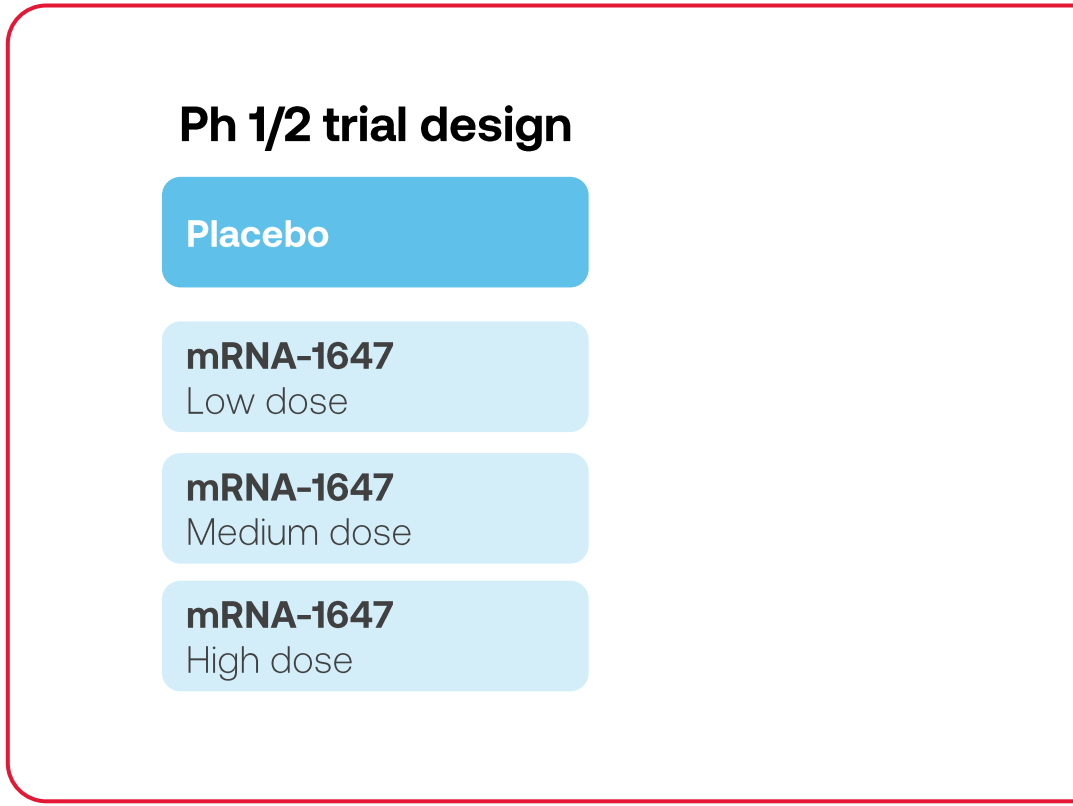
- **Ease of implementation** into existing (ACIP) vaccination schedule for this age group



https://www.cdc.gov/nchs/products/databriefs/db90.htm
NHANES (National Health and Nutrition Examination Survey)

CMV vaccine (mRNA-1647) Phase 1/2 study in adolescents has begun enrollment

- Phase 1/2 open-label and placebo-controlled study to evaluate safety and immunogenicity in male and female participants at 9 to 15 years of age
- The study will include ~770 participants across ~70 sites globally
- Immunogenicity will be assessed against both epithelial cell and fibroblast cell infection



CMV vaccine (mRNA-1647) indication expansion studies

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Sources: (1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8453618/

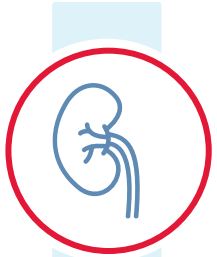
CMV is a major health burden in the transplant population

Risks associated with CMV infection post SOT/HSCT[1]

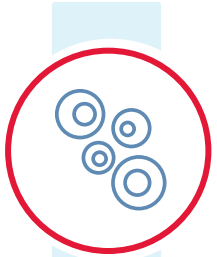
- Graft rejection
- End-organ CMV disease (EOD)

Unmet need:

- No approved vaccines against CMV for post-transplant
- High cost and toxicity of antiviral prophylaxis



47K
Solid Organ Transplantation (SOT)[2]



23K
Hematopoietic Stem Cell Transplantation (HSCT)[3]

~70K transplants in the US annually

(1) https://pubmed.ncbi.nlm.nih.gov/32603496/ (2) https://insights.unos.org/OPTN-metrics/. Data for year 2023. (3) https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics Data for year 2021

CMV infection is a frequent complication after transplantation

Infection occurs due to transmission from the transplanted organ, reactivation of latent infection, or after a primary infection in seronegative patients

Incidence of CMV disease risk[3]		
	Donor+/recipient –	**Recipient +**
Kidney	0-50%	2-15%
Liver	8-40%	0-4%
Lung	10-33%	7-19%
Heart	0-25%	0-14%
	Recipient -	**Recipient +**
Allogeneic HSCT[4]	0-12%	30-80% (median 37%)

The harmful effects of CMV in transplant recipients result from:

- The direct effect of the virus on various organs and systems, mainly causing pneumonia, gastrointestinal tract disease, hepatitis, encephalitis, and retinitis[1]
- The indirect immunomodulatory effects of the virus, predisposing patients to graft rejection and other opportunistic infections[2]

In solid organ transplantation (SOT), **the greatest risk factor for CMV disease is a serological mismatch between the donor and the recipient** (the recipient is CMV seronegative and the donor is seropositive)

1. Azevedo, Luiz et al., *Clinics (Sao Paulo)* (2015), https://doi.org/10.6061/clinics/2015(07)09
2. Haidar, Ghady et al., *J Infect Dis* (2020), https://doi.org/10.1093/infdis/jiz454
3. Limaye, Ajit et al., *ASM Journals* (2020), https://doi.org/10.1128/CMR.00043-19
4. Styczynski, Jan, *Infect Dis Ther.* (2018), https://doi.org/10.1007/s40121-017-0180-z

CMV vaccine (mRNA-1647) Phase 2 proof-of-concept study in allogeneic hematopoietic cell transplant (HCT) patients; enrollment ongoing

- **Phase 2, placebo controlled, single-center proof-of-concept (POC) study** evaluating efficacy, safety and immunogenicity of mRNA -1647 in patients undergoing HCT
- The study will recruit CMV-seropositive patients who have gone high-risk allogeneic HCT
- Primary outcome measure is time to first occurrence of an CS-CMVi event measures by initiation of antiviral therapy
- The study will recruit approximately 224 patients with a 1:1 randomization
- We are enrolling participants after immune reconstitution with 3 doses over an accelerated schedule and following subjects over 1 year

Medical and scientific presentations

ECSMID 2025 (safety & immunogenicity; 36 months)

https://s29.q4cdn.com/435878511/files/doc_presentations/2025/Apr/14/CMV-Poster-P202-IA-EXT-36-Month.pdf

IDWeek 2023

https://s29.q4cdn.com/435878511/files/doc_presentations/2023/Oct/14/cmv-2023-idweek-presentation.pdf

Forward looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements regarding: the potential of mRNA-1647 to prevent CMV infection, including congenital CMV infection; expected market opportunity; development candidate activities and clinical trials; expected timing of the Phase 3 readout; and the potential for vaccine efficacy readout in 2025. In some cases, forward -looking statements can be identified by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “aims,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology, although not all forward -looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties and other factors, many of which are beyond Moderna’s control and which could cause actual results to differ materially from those expressed or implied by these forward - looking statements. These risks, uncertainties and other factors include those described in Moderna’s most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna’s current expectations and speak only as of the date referenced on the first page.