ACIP CMV Vaccine Workgroup
Initial Considerations for CMV Vaccine Policy

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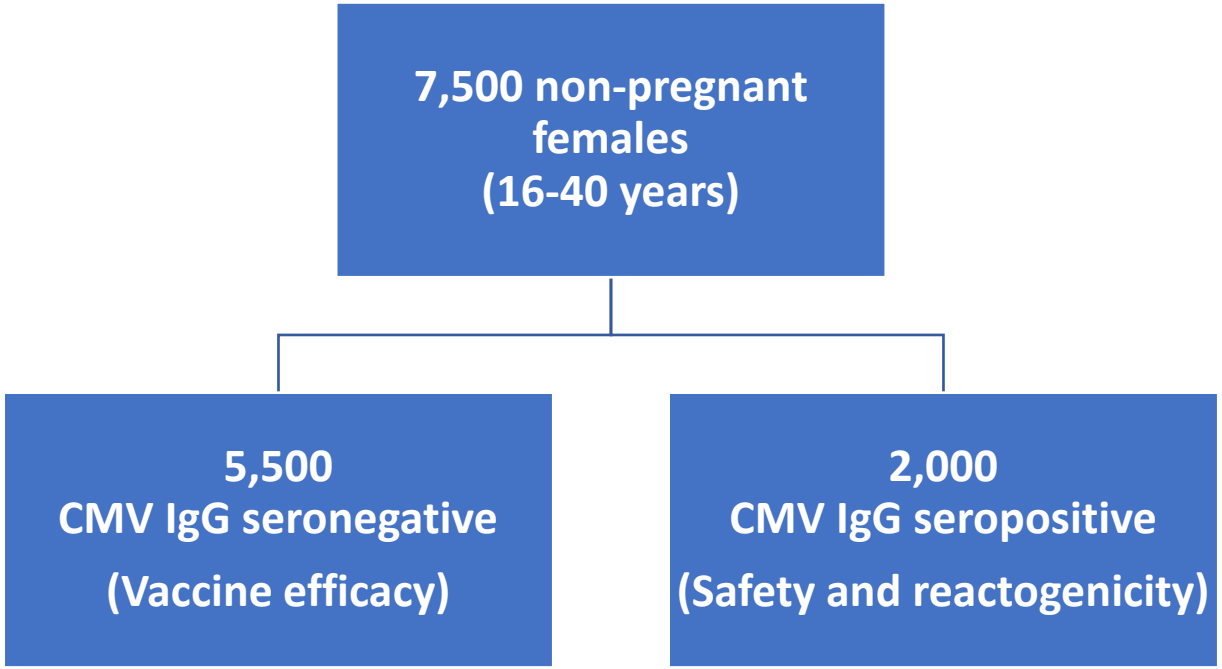
CMV as a public health problem

- **The burden of congenital CMV is substantial but awareness is low**
  - Need to assess vaccine acceptability and feasibility of implementation
- **Primary maternal infections have a higher risk of vertical transmission, are estimated to cause most cCMV infections in the U.S., and result in more severe cCMV disease if occurring in the first trimester of pregnancy**
  - Vaccination before pregnancy, and long-lasting protection throughout childbearing years would be needed
  - CMV seroprevalence increases with age, but certain groups of the population already have high seroprevalence by adolescence

Moderna mRNA-1647 CMV vaccine

- **CMV gB and pentamer complex (gH, gL, UL128, UL130, UL131)**
  - 3 doses: 0, 2, 6 months after the first dose

- **Phase 3 trial (ongoing)**
  - *Randomization*: 1:1 vaccine:placebo, within each serostatus group, and stratified by age group
  - *Follow-up*: 24 months after the 3rd dose, with an extension to 48 months for a subset of the cohort



Study Details | A Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1647 Cytomegalovirus (CMV) Vaccine in Healthy Participants 16 to 40 Years of Age | ClinicalTrials.gov

Moderna mRNA-1647 CMV vaccine – clinical trial endpoints

Primary

- **Vaccine efficacy against primary infection in CMV-seronegative** (vaccine vs. placebo recipients) from 28 days up to 24-48 months after the 3rd dose
  - Primary infection: seroconversion from negative to positive for IgG against CMV antigens **not** included in vaccine
- **Safety and reactogenicity in all participants**

Secondary

- **Immunogenicity** at day 1 and months 3, 7, 12
- **Immune persistence** at months 18, 24, and 30
  - *gB and pentamer* antigen-specific neutralizing antibody titers and binding antibody concentrations in CMV-seronegative vaccine vs. placebo recipients

Exploratory

- Symptomatic primary infection, urinary CMV excretion (CMV-seropositive)

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WG interpretation of data from Moderna's mRNA-1647 vaccine phase 1 and phase 2 trials

- **No safety concerns**
- **Immunogenicity –** need to better understand differences in neutralizing antibody levels against epithelial cell and fibroblast entry; antibody-dependent cellular cytotoxicity and phagocytosis (ADCC & ADPC)
- **Long-term protection –** some data showing antibody persistence through at least 3 years following dose 1

WG considerations on Moderna's mRNA-1647 vaccine phase 3 trial

- Moderna's planned vaccine indication is for *non-pregnant* females 16-40 years; 3-dose series (6 months)
- Efficacy will be assessed only for primary infection among initially CMV-seronegative subjects
- Data on duration of immunity will be limited; need to ensure protection before pregnancy and throughout childbearing age years
- Efficacy against vertical transmission, cCMV infection or disease?
- Better understanding of correlates of protection against vertical transmission is needed
- Benefit to CMV-seropositive individuals yet unknown while serological testing prior to vaccination would pose implementation challenges
- Groups considered for vaccine recommendations might change as data from future clinical trials (e.g. adolescents, transplant patients) become available

Next steps

Evidence to Recommendation (EtR) Domains

Conclusions

- **An effective CMV vaccine could reduce cCMV disease burden**
  - Over 16,000 children born with cCMV infection in the U.S. every year; nearly 3,000 with cCMV disease
- **mRNA-1647 CMV vaccine candidate**
  - Shown to be safe and immunogenic in phase 1 and 2 studies
  - Efficacy data on prevention of primary CMV infection in CMV-seronegative women 16-40 years of age from ongoing phase 3 trial expected next year
  - Need to ensure protection against CMV infection before pregnancy to reduce vertical transmission
- **Low awareness and potential need for serological screening might pose implementation challenges**
- **The CMV ACIP WG will meet regularly to review data and develop CMV vaccine policy options**

Acknowledgments - ACIP CMV WG Members

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