

**National Institute of Allergy and Infectious Diseases (NIAID)
COVID-19 VACCINE DATA AND SAFETY MONITORING BOARD**

September 18, 2020

MEETING SUMMARY

The NIAID COVID-19 Vaccine Data and Safety Monitoring Board (DSMB) met via teleconference on September 18, 2020 to perform a safety review of mRNA-1273 (P301/MODERNA). NIAID DSMB Executive Secretary Sally Hunsberger, Ph.D., Division of Clinical Research, welcomed Board members in attendance: Richard J. Whitley, M.D., (Chair); Abdel Babiker, Ph.D.; Susan Smith Ellenberg, Ph.D.; Alan Fix, M.D., M.S.; Marie R. Griffin, M.D., M.P.H.; Steven Joffe, M.D., M.P.H.; Jorge Kalil, M.D.; Myron Levine, M.D.; Malegapuru William Makgoba, MB., ChB; DPhil., FRCP and Anastasios A. Tsiatis, Ph.D. Lisa Angeline Cooper, M.D., M.P.H., FACP was not in attendance. Also, in attendance was Martha A. Nason, Ph.D., back up NIAID Executive Secretary (open session only).

**Closed Session was attended by DSMB Members, NIAID DSMB Executive Secretary and unblinded statistician. Executive closed session was attended by DSMB Members and NIAID DSMB Executive Secretary. Both session attendance was in accordance with the Vaccine COVID DSMB Charter. All other participants attended the open session discussions only.*

(mRNA-1273-P301/ MODERNA)
A PHASE 3, RANDOMIZED, STRATIFIED, OBSERVER-BLIND, PLACEBO
CONTROLLED STUDY TO EVALUATE THE EFFICACY, SAFETY, AND
IMMUNOGENICITY OF mRNA-1273 SARS CoV-2 VACCINE IN ADULTS AGED 18
YEARS AND OLDER

Protocol Team Participants:

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Brett Leav, M.D., Medical Lead, Moderna ^(O)

Conor Knightly, M.P.H., Senior Director/ Clinical Operations Lead, Moderna ^(O)

Honghong Zhou, Ph.D., Senior. Director/ Biostatistics Lead, Moderna ^(O)

Melissa Rossi, M.S., Senior Director/ Pharmacovigilance Lead, Moderna ^(O)

(b) (6) Moderna ^(O)

Jacqueline M. Miller, M.D., F.A.A.P., Senior Vice President/ Therapeutic Area Head, Moderna ^(O)

Shu Han, Ph.D., Head of Biostatistics, Moderna ^(O)

Lindsey Baden, MMSc., M.D., Co-Coordinating Investigator, CoVPN ^(O)

Hana El Sahly, M.D., Co-Coordinating Investigator, CoVPN ^(O)

Brandon Essink, M.D., Co-Coordinating Investigator, Meridian Research Network ^(O)

Larry Corey, M.D., HVTN Network Leadership, CoVPN ^(O)

Holly E. Janes, Ph.D., Statistician, CoVPN ^(O)

(b) (6) PPD ^(O)

Weiping Deng, Ph.D., Director/ Biostatistics Lead for P301, Moderna ^(O)

(b) (6) PPD ^(O)

Julie Ledgerwood, D.O., Investigator, Vaccine Research Center, NIAID ^(O)

Tatiana Beresnev, M.D., MSHS, Medical Monitor, OCRA, DMID ^(O)

Laura Polokowski, M.D., M.S.P.H., HIV Vaccine Research Program, NIAID ^(O)

Julia Hutter, M.D., M.P.H., DAIDS Medical Officer ^(O)

Mamodikoe Makhene, M.D., Medical Officer, Division of Microbiology and Infectious Diseases, NIAID ^(O)

Mary Marovich, M.D., Director, Vaccine Research Program, DAIDS, NIAID ^(O)

Emily J. Erbeling, M.D., M.P.H., Director, Division of Microbiology and Infectious Diseases, NIAID ^(O)

Others Attending:

Sally Hunsberger, Ph.D., NIAID Executive Secretary ^(C)

Martha Nason, Ph.D., Back Up NIAID Executive Secretary ^(O)

Delta Saint-Vil, DSMB Project Manager, Workforce Operations, Communications, and Reporting Branch, NIAID ^(O)

Yin Li, Management Analyst, Division of Clinical Research, NIAID ^(O)

Conflicts of Interest:

All DSMB members confirmed in writing that they had no financial or professional conflicts with this study.

Date of This Review: September 18, 2020

Date of Previous Reviews: August 28, 2020; July 21, 2020; June 30, 2020

Purpose of This Review: This was a safety review of mRNA-1273 (P301/MODERNA)

^(O) Participated in Open Session only

^(C) Unblinded Participant/Statistician (Closed Session)

Primary Objectives:

1. To demonstrate the efficacy of mRNA-1273 to prevent COVID-19.
2. To evaluate the safety and reactogenicity of 2 injections of the mRNA-1273 vaccine given 28 days apart.

Secondary Objectives:

1. To evaluate the efficacy of mRNA-1273 to prevent severe COVID-19.
2. To evaluate the efficacy of mRNA-1273 to prevent serologically confirmed SARS-CoV-2 infection or COVID-19 regardless of symptomatology or severity.
3. To evaluate VE against a secondary definition of COVID-19.
4. To evaluate VE to prevent death caused by COVID-19.
5. To evaluate the efficacy of mRNA-1273 to prevent COVID-19 after the first dose of IP.
6. To evaluate the efficacy of mRNA-1273 to prevent COVID-19 in all study participants, regardless of evidence of prior SARS-CoV-2 infection.
7. To evaluate the efficacy of mRNA-1273 to prevent asymptomatic SARS-CoV-2 infection.

Observations:

1. The board recognizes the immense challenge the study team is undertaking to accrue participants, collect, query, and clean data, and protect participant safety all at warp speed with the country watching. The board congratulates the team on performing these tasks with speed while maintaining the highest level of scientific rigor.
2. The board agrees and is pleased with the concrete steps the study team has taken to increase accrual of minority populations and encourages continuation of these efforts.

Recommendations:

1. The board would like to be notified of participant deaths and SUSARs as soon as the information is available.
2. The board requests terminology for safety events be consistent across reports and usage of preferred terms be consolidated into one type of clinical event. For example, varying preferred terms are used for hypertension throughout the report.
3. The board would like a description of the process of unblinding safety events. In particular, who is unblinded and what specific criteria are used to trigger unblinding. The board would like to encourage the study team to emphasize enrollment of minority participants older than 65 since currently enrollment is lagging in this group.

Conclusion: Continue the study as planned.

Next Planned Review: The board would like to review the study in one month.

Recommendations:

1. The board would like to be notified of participant deaths and SUSARs as soon as the information is available.

Sponsor's response: Moderna's Safety Vendor, IQVIA, will provide MedWatch reports for all deaths and SUSARs to the DSMB as they occur.

Moderna would like to clarify the DSMB's responsibility in the review of these reports. Should Moderna expect a response from the DSMB to each of these reports or can we assume that unless a response is received the DSMB has no concerns?

2. The board requests terminology for safety events be consistent across reports and usage of preferred terms be consolidated into one type of clinical event. For example, varying preferred terms are used for hypertension throughout the report.

Sponsor's response: Moderna applies MedDRA codes based on standard conventions and AE as reported in the CRF by investigators (MedDRA Point to Consider). To address the specific concern noted by the DSMB, when summarizing adverse events of interest, Moderna will endeavor to use standardized or customized MedDRA queries (SMQ or CMQ) to provide the Board with a consolidation of Preferred Terms reflecting the particular pathophysiologic concern. .

3. The board would like a description of the process of unblinding safety events. In particular, who is unblinded and what specific criteria are used to trigger unblinding.

Sponsor's response: Unblinding of a SUSAR is required for regulatory reporting purposes. Access to unblinded information within the Moderna Global Safety Database, Argus, is limited to the IQVIA case processing team and IQVIA PV Regulatory reporting team only. The IQVIA case processing team will not share the treatment allocation result with other IQVIA or Moderna staff who are involved in the conduct or analysis of the Clinical Trial. The Argus database maintains the blind based on user role. The only roles with access to treatment code within Argus is the role of IQVIA case processing team and IQVIA PV Regulatory reporting team who are not involved in the conduct or analysis of the Clinical Trial.

The board would like to encourage the study team to emphasize enrollment of minority participants older than 65 since currently enrollment is lagging in this group.

Sponsor's response: The challenge has been that the upper limit of our stratification based in part on older age, created a challenge enroll more older minority subjects in the waning period of study recruitment. We have tried to increase the numbers of older minority participants by amending the study protocol to increase the stratification limit from 40 to 50%.