Evaluation of a heterologous booster vaccine regimen: Pfizer-BioNTech BNT162b2 mRNA booster vaccine following priming with Novavax NVX-CoV2373

Tara Babu, MD, MSCI[1], R. Scott McClelland, MD, MPH[1], Christine Johnston, MD, MPH[1], Stacy Selke, MS[1], Xiaoying Shen[2], DVM, PhD, Dilpreet Singh, BS[1], Morissa Pertik, PA-C[1], Jina Taub, ARNP[1], Dana Varon, ARNP[1], Thepthara Pholsena, NP[1], Britt Murphy, ARNP[1] Jessica Moreno, BS[1], Mark Drummond, BS[1], Lindsey McClellan, BS[1], Alyssa Braun, BS[1], Matthew Seymour, BS, MPH[1], Jessica Heimonen, BS, MPH, Kirsten Hauge, BS, MPH[1], Chloe E. Wilkens, BS[1], Chris McClurkan, BS[1], Erin A. Goecker, MS[1], Kerry Laing, PhD[1], David M. Koelle, MD[1], David Montefiori, PhD[3], Alex Greninger, MD, PhD, MS, MPhil[1], Anna Wald, MD, MPH[1,4,5]

[1] Department of Medicine, University of Washington, Seattle, WA, [2]Department of Surgery, Duke University, Durham, NC, [3]Human Vaccine Institute, Duke University, Durham, NC, [4]Department of Laboratory Medicine & Pathology, University of Washington, Seattle, WA, [5]Vaccines and Infectious Diseases Division, Fred Hutchinson Cancer Research Center, Seattle, WA

Background

- Novavax protein-based NVX-CoV2373 vaccine has been shown to be safe and effective for prevention of COVID-19.
- The immune response after 2 doses of Novavax protein-based NVX-CoV2373 followed by the Pfizer-BioNTech BNT162b2 vaccine has not been evaluated.
- Emerging data suggest that providing boosters different from the primary series (heterologous vaccination) may provide a broader immune response than boosting with the same vaccine (homologous vaccination).
- In 9/2021, the CDC recommended the Pfizer-BioNTech BNT162b2 30-µg mRNA booster vaccine to all people > 6 months post primary series, including those participating in clinical trials.

Methods

- We conducted an observational study in persons who received 2 doses of Novavax protein-based NVX-CoV2373 vaccine, in a Phase 3 clinical trial, and received a Pfizer BNT162b2 booster vaccine under EUA >6 months after primary series.
- Study visits: pre-booster, D18, D34, D91 (M3), D181 (M6).
- Anti-nucleocapsid (N) IgG and anti-Spike (S) IgG (Roche), were performed at all visits.
- Neutralization assays using pseudotype virus for variant strains of SARS-CoV-2 were performed at D0, D18, and D181
- The Oxford T-Spot COVID Discovery Kit against Spike protein was conducted at D0 and D34.
- Wilcoxon rank test was performed between pre-booster and each subsequent visit for Anti-S-IgG and D0 and D34 for T-spot assay and GMT fold change was calculated.

Table 1. Demographics and Clinical Characteristics

Characteristics	N=30 (%)
Median age in years (range)	47 (29-67)
Women	17 (57)
Hispanic ethnicity	6 (20)
Race	
White	21 (70)
Asian	3 (10)
Other	3 (10)
More than one race	3 (10)
Booster timing (median)	
10.4 months	16 (54)
7 months	14 (46)
Prior SARS-CoV-2 infection	9 (30)

Figure 2. Anti-S-IgG in participants who remained uninfected, p-value: 0.001 comparing D0 and D181

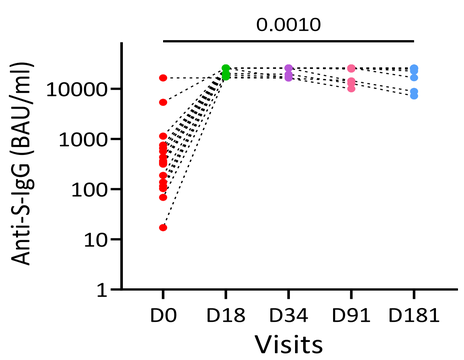


Figure 3. T cell response to S peptide cocktail in participants who remained uninfected; p-value 0.0003 comparing D0 and D34

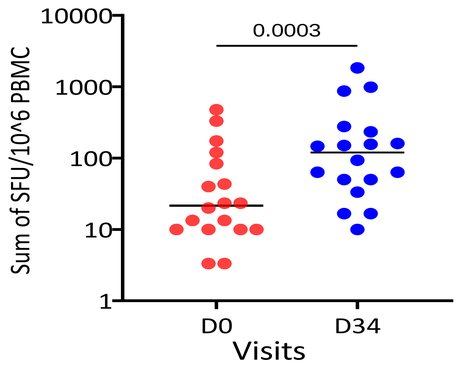
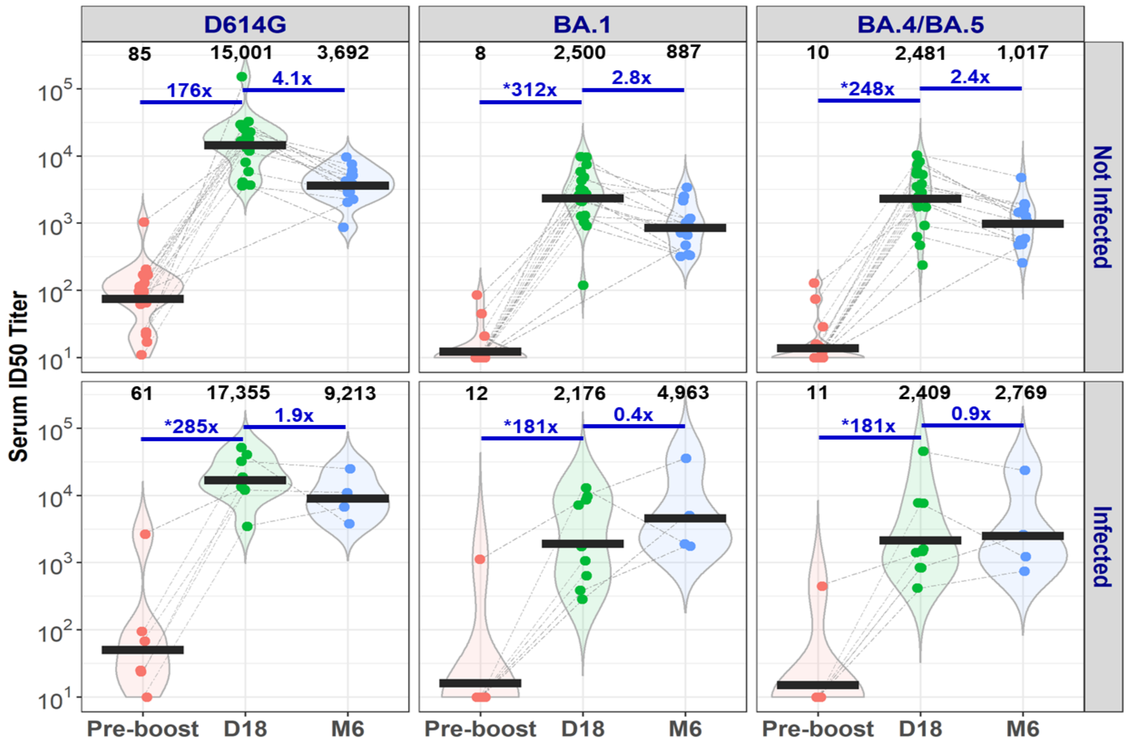


Figure 4. Pseudovirus ID50 titers and fold reduction in ID50 GMT compared over time for D614G, BA.1, BA./BA.5 as stratified by COVID-19 infection, * Fold difference at pre-boost cannot be accurately assessed due to large negative samples for BA.1 and BA.4/BA.5 pre-boost



Results

- Anti-S-IgG: Titers were boosted ~84 fold from D0 to D18 and there was a 1.2-fold decrease from D18 to month 6.
- T cell response: There was a 3.4-fold increase in response from D0 to D34.
- Neutralization assays: The ID50 titers were boosted >150 fold for BA.1 and BA.4/BA.5 variants at D18 compared to pre-boost. In uninfected participants, from D18 to M6, there was a 4.1-fold drop in ID50 titer D614G and 2.4-fold drop for BA.4/BA.5.
- This heterologous vaccine regimen resulted in a robust and durable antibody response at 6 months post-booster vaccine against BA.1 and BA.4/BA.5.

Conclusions

- Two doses of NVX-CoV2373 followed by Pfizer BNT162b2 booster regimen resulted in a robust and durable antibody response at 6 months post-booster against BA.1 and BA.4/BA.5.
- Protein vaccine priming followed by mRNA vaccine boosting and/or delayed boosting may have contributed to the robust immune response following the Pfizer BNT162b2.

Acknowledgments

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