PUBLICATION CARD

The Novavax Heterologous Coronavirus Disease 2019 Booster Demonstrates Lower Reactogenicity Than Messenger RNA: A Targeted Review

Nov 2023

Authors*: Anthony M. Marchese, Matthew Rousculp, John Macbeth, Hadi Beyhaghi, Bruce T. Seet, Seth Toback

Journal: *The Journal of Infectious Diseases;* **DOI**: https://doi.org/10.1093/infdis/jiad519

*All authors are salaried employees of Novavax, Inc. and hold Novavax stock

OBJECTIVE

- To conduct a targeted review of the reactogenicity of authorized/ approved mRNA and protein-based COVID-19 vaccines, as demonstrated by clinical trials and real-world evidence[8]

STUDY LIMITATIONS

- Findings of this study cannot be directly applied to all protein-based vaccines, as different adjuvants may lead to varying reactogenicity[8]
- The study was not designed to compare between vaccine groups
- The study was not blinded and randomized[8]
- mRNA-1273 vaccine booster dose studied was 100ug which is twice the currently approved dose in use (50ug)
- No homologous NVX-CoV2373 regimens were included in the study design[8]

METHODS

Search strategy[8]

- Database: BIOSIS Previews, Embase, Embase Preprints, Medline, and publicly available content searched using ProQuest Dialog

Time period[8]

- Database include articles up to July 2023

Inclusion criteria[8]

- Clinical trials/real-world studies assessing reactogenicity of NVX-CoV2373 and/or mRNA boosters after an mRNA primary series vaccination regimen
- Studies reporting local/systemic AEs after booster doses

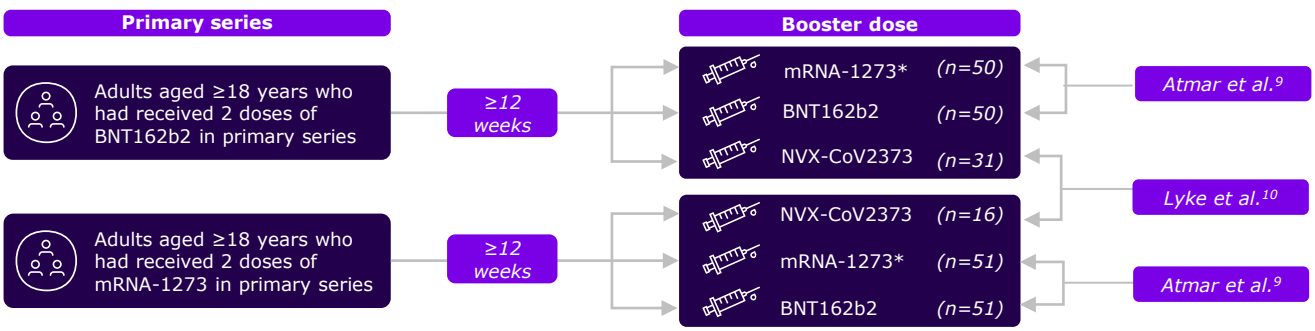
Exclusion criteria[8]

- Studies that did not include participants who received an mRNA primary series vaccination
- Studies focused solely on immunocompromised populations
- Studies conducted on non-human subjects

RESULTS

Selected publications based on NCT04889209 clinical trial[8]

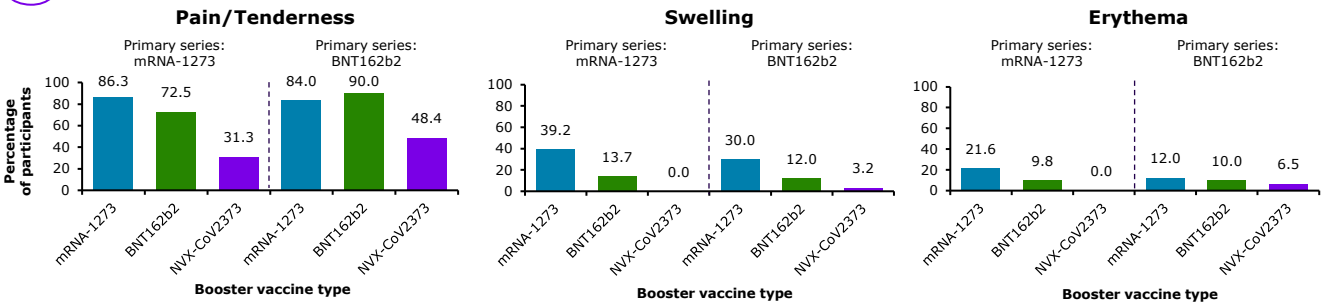
- NCT04889209 is an open-label, non-randomized, adaptive-design trial evaluating the safety, reactogenicity, and immunogenicity of a delayed (≥12 weeks) homologous and heterologous COVID-19 booster doses following primary series administration of approved COVID-19 vaccines
- The study has two publications (Atmar et al.[9] and Lyke et al.[10]), relatively small sample sizes, with NVX-CoV2373 recipients being slightly younger than those receiving mRNA boosters
- For this targeted review, data from Atmar et al.[9] and Lyke et al.[10] on participants who received an mRNA primary series and either an mRNA or protein-based booster were summarized as a percentage of participants reporting any symptom and plotted together
- Reactogenicity data were collected using a memory aid survey, documented for 7 days post-vaccination, with severity assessed based on the highest recorded symptom. Delayed-onset local reactions were monitored for 14 days



*The mRNA-1273 vaccine booster dose studied was higher (100 µg) than the currently approved dose of 50 µg
mRNA-1273 = 100 µg dose; BNT162b2 = 30 µg dose; NVX-CoV2373 = 5 µg rS protein + 50 µg Matrix-M adjuvant

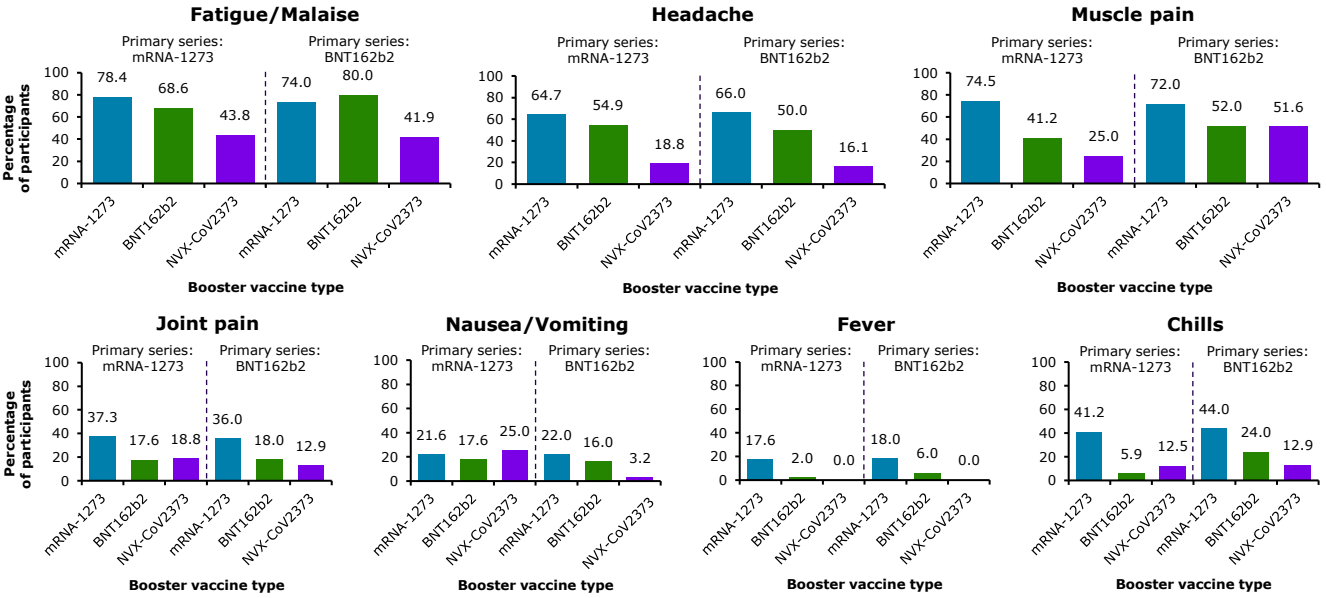
RESULTS

Local reactogenicity following booster vaccination[8]



- The NVX-CoV2373 booster exhibited lower rates of local reactions such as pain/tenderness, swelling, and erythema
- Pain/tenderness was most frequent in homologous mRNA booster groups, particularly in those receiving three doses of BNT162b2 (90%) or mRNA-1273 (86.3%), while heterologous NVX-CoV2373 showed the lowest frequency (31.3% and 48.4%, mRNA-1273 and BNT162b2 primary series respectively)

Systemic reactogenicity following booster vaccination[8]



- This study analyzed outcomes from NCT04889209, and incorporated data from multiple studies, including COV-BOOST (ISRCTN73765130), Com-COV2, and real-world data from the U.S., Canada, Japan, Australia, and South Korea[11-16]
- Across these studies, similar patterns of vaccine-induced reactogenicity were observed, reinforcing the findings from NCT04889209[11-16]

Glossary: ×2, 2-dose primary series; AE, adverse events; BNT, BioNTech; COVID-19, coronavirus disease 2019; mRNA, messenger ribonucleic acid; NVX, Novavax; rS, recombinant spike; SD, standard deviation; U.S, United States.

Reference: 1. Al-Obaydi S, et al. *PLoS One*. 2022;17:e0272691; **2**. Chrissian AA, et al. *Vaccine*. 2022;40:3174–81; **3**. Long S, et al. *Front Public Health*. 2022;10:929407; **4**. Rief W. *JAMA Health Forum*. 2021;2:e210804; **5**. Breeher LE, et al. *J Occup Environ Med*. 2022;64:6–9; **6**. Cohen DA, et al. *Medicine (Baltimore)*. 2022;101:e28839; **7**. Sutton N, et al. *Expert Rev. Vaccines*. 2022;21:1301-18; **8.** Marchese AM, et al. *J Infect Dis*. 2024;230(2):e496–e502; **9**. Atmar RL, et al. *N Engl J Med*. 2022;386:1046–57; **10**. Lyke KE, et al. *NPJ Vaccines*. 2023;8:98; **11**. Munro APS, et al. *Lancet*. 2021;398:2258–76; **12**. Stuart ASV, et al. *Lancet*. 2022;399:36–49; **13**. Rousculp M, et al. *medRxiv*. 2023; **14**. Ministry of Health Labor and Welfare of Japan. 2022; **15**. Salter SM, et al. *Vaccines (Basel)*. 2022;10:2017; **16**. Kim SH, et al. *J Int Adv Otol*. 2023;19:228–33.