

Supplemental Online Content

Krantz MS, Kwah JH, Stone Jr CA, et al. Safety evaluation of the second dose of messenger RNA COVID-19 vaccines in patients with immediate reactions to the first dose. *JAMA Intern Med*. Published online July 26, 2021. doi:10.1001/jamainternmed.2021.3779

eMethods.

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

This was a multicenter, retrospective study conducted by Massachusetts General Hospital, Brigham and Women's Hospital, Vanderbilt University Medical Center (VUMC), Yale School of Medicine (YSM), and University of Texas Southwestern Medical (UTSW) Center from 1/1/2021 through 3/31/2021. Included patients had an immediate and potentially allergic reaction specified as: (1) onset of symptoms within 4 hours of dose one of the Pfizer-BioNTech or Moderna mRNA COVID-19 vaccine, (2) at least one potentially allergic symptom, and (3) in-clinic or tele-health assessment by Allergy/Immunology performed after dose one of an mRNA COVID-19 vaccine. Potential allergic symptoms and signs were: hives; swelling in the lips, eyes, tongue, or throat; throat tightness; metallic taste; numbness; tingling; flushing; erythema; tachycardia; hypertension; wheezing; shortness of breath; nausea or vomiting; abdominal pain; dizziness; lightheadedness; hypotension; hypoxia, or bradycardia.

Allergy/Immunology assessment occurred in-person or by tele-health. A shared, but not prospectively defined, clinical approach was used by the sites that included obtaining dose one reaction history (timing, symptoms, severity) and any prior evidence of possible sensitization to polyethylene glycol (PEG) and/or polysorbates.¹ Excipient skin testing with PEG was used variably in individuals Allergy/Immunology deemed higher risk. Patients were excluded from second dose administration if they had evidence of severe immediate reaction with objective supportive signs of allergy and/or evidence of IgE-mediated mechanism (positive PEG skin testing, elevated tryptase test). Second doses were administered with or without Allergy/Immunology supervision present depending on the site with a 30 minute observation. All second dose mRNA vaccine administrations were given according to the FDA emergency use authorization, without dilution or split dosing, except for the first patient evaluated by Yale School of Medicine who was given the second dose of vaccine in two steps. For any individuals who did not have their vaccination observed by Allergy/Immunology, follow-up phone calls were made to elicit dose two clinical details.

Electronic health records were reviewed for patient demographics, vaccine dose one history (manufacturer, reaction symptoms, reaction timing, and treatment), Allergy/Immunology clinical assessment (including whether excipient skin testing was performed), and vaccine dose two administration outcomes (receipt, timing of receipt, premedication, reactions symptoms, and treatment). Episodes were also scored using the Brighton² and the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network (NIAID/FAAN)³ criteria. Confirmed anaphylaxis required meeting at least one of these two criteria.

The primary outcome was dose two tolerance, defined as either: 1) no immediate symptoms after second dose administration or 2) symptoms that were mild, self-limited, and/or resolved with antihistamines alone. Second dose mRNA COVID-19 vaccine tolerance was determined by either Allergy/Immunology observation of second dose or confirmed by patient in follow-up if vaccine was administered outside of the Allergy/Immunology clinic.

We report descriptive statistics such as means with standard deviations for continuous variables and numbers with frequencies for categorical variables. This study was reviewed and approved by the Mass General Brigham Human Research Committee with waiver of informed consent (study #2020P0040608), and institutional review boards (IRB) at other participating sites (VUMC IRB #161455, YSM IRB #2000029888, and UTSW IRB #32703).

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