NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: A Post-Emergency Use Authorization Observational Cohort Study to Evaluate the Safety of the Pfizer-BioNTech COVID-19 Vaccine in US Healthcare Workers, Their Families, and Their Communities

Date: 22 June 2021

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Keywords: COVID-19, vaccine, observational

Rationale and background: Pfizer-BioNTech COVID-19 vaccine was approved for emergency use authorization (EUA) to prevent Coronavirus Disease 2019 (COVID-19) for individuals 16 years of age and older. Detailed distribution plans for the COVID-19 vaccine within the US are determined by local jurisdictions based on federal recommendations to prioritize vaccination of healthcare workers and people living in long term care facilities under an EUA. This study is designed to provide early real-world safety information on a cohort of vaccinated healthcare workers, their families, and their communities for two years after vaccination. This non-interventional study is designated as a PASS and is included in the US pharmacovigilance plan.

Research question and objectives: The research questions addressed by this study are a) what are the incidence rates of safety events of interest and other clinically significant events among persons vaccinated with the Pfizer-BioNTech COVID-19 vaccine in a cohort of US healthcare workers, their families, and their communities and b) how do those rates compare to expected rates of those events?

Primary study objectives:

- Estimate the real-world incidence of safety events of interest and other clinically significant events among US healthcare workers, their families, and their communities who are vaccinated with the Pfizer-BioNTech COVID-19 vaccine following Emergency Use Authorization.

Secondary objectives

- Evaluate whether vaccine recipients experience increased risk of safety events of interest and other clinically significant events post-vaccination.
- Estimate the incidence rates of safety events of interest and other clinically significant events among subcohorts of interest such as individuals who are pregnant, individuals who are immunocompromised, and stratified by age.

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Study design: This is a prospective observational cohort study of US healthcare workers, their families, and their communities, in which data are collected from participant self-report at regular intervals following vaccination, primarily using a secure, participant-facing web portal, as well as medical records for confirming the occurrence of safety events. The study period will be 30 months.

Setting: Participants will be recruited from three primary sources. The first is the Healthcare Worker Exposure Response and Outcomes (HERO) Registry Study, launched in April 2020 to characterize COVID-19 risk factors and outcomes among healthcare workers (HCWs) in the United States by the Duke Clinical Research Institute (DCRI). The second source of participants is from the Project Baseline Community Study platform operated by Verily. This study was launched in April 2019 by Verily Life Sciences and provides an opportunity to acquire, organize, analyze, and activate phenotypic data for a group of participants over time. The third source of participants is major health systems distributing Pfizer-BioNTech COVID-19 vaccine to its employees, their families, and community members as determined by local jurisdictional EUA rollout plans.

Subjects and study size, including dropouts: This study will aim to enroll and follow 20,000 vaccinated healthcare workers, their families, and their communities during a 30-month study period. The data for this interim report was cut for subjects enrolling before 29 April 2021, which was just prior to a study expansion in order to include more than health care workers.

Variables and data sources: The study will capture data through three primary mechanisms. First, participants will use a secure, participant-facing web-portal to provide information on COVID-19 vaccination, baseline characteristics, seeking of non-routine medical care (including hospitalization) and potential occurrence of safety events of interest. Secondly, a Call Center will be utilized to:

- Serve as a “rescue” mechanism to minimize incomplete data from non-response and loss to follow-up, and
- Request medical records for confirmation of the occurrence of safety events of interest.

This report summarizes participant-reported outcomes that are confirmed via medical record review by the DCRI Clinical Events Ascertainment CEA Confirmation Team. The full adjudication process is being finalized. In the interim, the CEA confirmation team has implemented a confirmation process whereby available medical records are reviewed to determine probable event status for further details). Full adjudication of events will be reported in future reports, after the adjudication process finalization.

Results: This interim report includes a descriptive analysis and participant-reported outcomes using data collected from 17 December 2020 through 29 April 2021. Of the 7824 consented participants, 2511 were eligible for inclusion in the primary analysis safety population (PASP) and 5313 were in the consented but not eligible for inclusion in the primary analysis safety population (CNPASP). The distribution of demographic

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characteristics, baseline characteristics, study withdrawals, medical history, and baseline medication use were similar between these populations. The PASP is primarily white (79.1%), female (70.3%), and not Hispanic (82.0%).

The incidence proportions of reported hospitalizations were numerically similar for the PASP and all consented population (ACP). In general, the proportion of the PASP reporting any safety event of interest was numerically similar to that of the ACP. Two deaths were reported (one in the PASP and one in the CNPASP); neither was COVID-19 related. Immunocompromised participants in the PASP reported more frequently any safety event of interest (21.5%) than non-immunocompromised participants (12.1%).

Discussion: Of the initial 7824 participants enrolled in HERO-Together, population demographics are consistent with expected distributions given the healthcare worker inclusion criterion at the time of this data cut, the online nature of the study and the requirement for vaccination prior to enrollment.[2] While the inclusion criteria for HERO-Together are intentionally broad, racial/ethnic diversity of the initial population is lower than anticipated, with the majority of participants identifying as white. The number of participant-reported events to date was low for most pre-specified AESIs, and the majority of events were still in the process of full adjudication. Therefore, all AESIs in this report should be interpreted with caution. Source documentation will be requested for these events to determine occurrence of any AESIs consistent with study definitions.

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FDA-CBER-2021-5683-1073738

Document Approval Record

Document Name:	CT24-WI-GL15-RF01 1.0 NI Study Report Abstract
Document Title:	C4591008 Interim

Signed By:	Date(GMT)	Signing Capacity
Madsen, Ann	22-Jun-2021 17:04:49	Manager Approval
McLaughlin, Margaret M	22-Jun-2021 17:51:57	Final Approval

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