NON-INTERVENTIONAL STUDY
FINAL REPORT ABSTRACT

Title: HERO-Together Boost: A Post-Emergency Use Authorization Observational Cohort Study to Evaluate the Safety of the Pfizer-BioNTech COVID-19 Vaccine

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Rationale and background: Pfizer-BioNTech COVID-19 vaccine was approved for emergency use authorization to prevent COVID-19 for individuals 16 years of age and older on 11 December 2020 and received full approval on 23 August 2022. HERO-Together Boost was a Post-Authorization Safety study.

Research question and objectives: What are the incidence rates of safety events of interest among persons vaccinated with the Pfizer-BioNTech COVID 19 vaccine in a US cohort?

Primary objective: To estimate the real-world incidence of safety events of interest among recipients of the Pfizer-BioNTech COVID-19 vaccine following emergency use authorization.

Secondary objective: To estimate the incidence rates of safety events of interest among subgroups of interest, including individuals who are pregnant, individuals who are immunocompromised, and individuals stratified by age.

Study design: This prospective observational cohort study was launched in August 2023 and the study period spanned approximately 18 months. Data were collected primarily through participant self-report via a secure web portal at regular intervals following vaccination. Efforts were made to confirm the occurrence of safety events resulting in hospitalization by medical record review. For a subset of hospitalizations, ancillary analyses explored the concordance between methods of event ascertainment (self-report, adjudication, or claims-based).

Setting: Participants in the United States self-enrolled remotely, recruited primarily by pharmacy email invitations.

Subjects and study size, including dropouts: A total of 13,623 individuals were screened; 10,269 met eligibility criteria and provided informed consent, comprising the All Consented Population (ACP). Among the ACP, a total of 1,230 consented and eligible participants enrolled within 10 days following their index vaccination and were included in the Primary Analysis Safety Population (PASP). The remaining 9,015 consented and eligible participants enrolled more than 10 days after their index vaccination and were included in Consented but not in Primary Analysis Safety Population (CNPASP). Completion rates were high across groups: 83.6% for PASP and 84.8% for CNPASP.

Variables and data sources: Data on vaccine exposure, covariates, and adverse events of special interest (AESIs) that were non-hospitalized or requiring hospitalization were self-reported through the secure participant portal. AESIs in this study were derived from a combination of the Priority List of AESIs from the Brighton Collaboration's Safety Platform for Emergency Vaccines Project updated in October 2022 AESI per the FDA-CBER Best Initiative, spontaneous reporting, and the framework from a preceding study (C4591008).

Participant-reported events were adjudicated by physician reviewers trained on the study protocol and safety event definitions.

Results: The study population was primarily White (82.2%), female (58.7%), not Hispanic or Latino (87.6%) with a mean age of 5 4.3 years ranging from 18 to 88 years and had a low prevalence of comorbidity at Baseline. The incidence proportions of both non-adjudicated (< 1.0%) and confirmed hospitalizations (< 1.0%) due to AESIs was low. Non-hospitalized AESIs were also relatively uncommon, reported by approximately 5.2% of study participants, with non-severe allergic reactions being the most frequent event (1.5% of study participants). All other non-hospitalized AESIs occurred in < 1.0% of participants. Analysis of incidence rates of AESI among subgroups of interest estimate higher rates of confirmed hospitalization among recipients of the Pfizer-BioNTech COVID-19 vaccine who were in the subgroups of immunosuppressed or 70+ years of age, than in strata of immunocompetent or younger ages, respectively.

There was poor concordance (kappa=0.26) and a low positive specific agreement (0.33) between claims-based methods and medical record review adjudication for safety event confirmation.

Discussion: This study provides comprehensive real-world safety information about the Pfizer-BioNTech COVID-19 vaccine, with evidence to support a low (< 1%) incidence proportion of AESI occurrence. The study allowed for enrollment up to 90 days following vaccination, which may introduce the potential for preferential self-enrollment of individuals experiencing an AESI (or early symptoms of an AESI). To mitigate this, the PASP was restricted to individuals who enrolled within 10 days following their index dose. Although smaller in size, PASP demographics and medical histories were similar to the CNPASP, supporting the use of the ACP as a representative sample. Overall, rates of confirmed hospitalization after receipt of the index dose of COVID-19 vaccine in the HERO-Together Boost study were markedly less than reported by the external sources. While the potential for missing data by relying on patient-report was a limitation, this was mitigated by employing Call Center rescue, email reminders, ongoing communications from the study team, and data-entry checks. In addition, as a voluntary study, results reflect a sample likely enriched with health-seeking individuals, which may reduce event risk and limit generalizability.
Concordance between claims-based methods and adjudication in the study was low, highlighting limitations of relying on claims data alone to confirm safety events. While open claims may supplement medical record review by identifying potential events not captured through other means, the low agreement underscores the importance of medical record review and adjudication as the gold standard for confirming AESIs in real-world settings.

Conclusion: Overall, AESIs were rare in this cohort, and the safety profile observed in the study is consistent with the well-established, favorable benefit-risk balance of the Pfizer-BioNTech COVID-19 vaccine demonstrated in prior randomized trials and post-authorization studies.

Marketing Authorization Holder(s): Pfizer Inc. and BioNTech SE

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