NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine

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Keywords: Pfizer-BioNTech COVID-19 vaccine; database study; active surveillance study; post-conditional approval safety study; non-interventional study

Rationale and background:
The Pfizer-BioNTech COVID-19 vaccine, tozinameran (Comirnaty®), a novel mRNA-based vaccine, has been authorised for use in several countries including the United States and European Union, for the prevention of COVID-19. Efficient and timely monitoring of the safety of the vaccine is needed. The overall goal of the study is to determine whether an increased risk of prespecified adverse events of special interest (AESIs) exists following the administration of at least one dose the Pfizer-BioNTech COVID-19 vaccine. This non-interventional study is designated as a Post-Authorization Safety Study (PASS) and is a commitment to EMA.

Research objectives:
The objectives are to describe the incidence rates and hazard ratios (HRs) risk estimates of 35 prespecified AESIs following the administration of at least one dose of the Pfizer-BioNTech COVID-19 vaccine in a non-matched vaccinated cohort, in a matched vaccinated cohort and a matched non-vaccinated cohort in six data sources in Europe.

Study design:
This post-authorisation active surveillance study of AESIs associated with the Pfizer-BioNTech COVID19 vaccine is using a retrospective cohort design involving multiple databases.

Setting:
For the implementation of this study covering the objectives of the second interim report, six electronic health care databases in Europe have been used: Agenzia Regionale di Sanita' della Toscana ARS, IT; Pedianet, IT; PHARMO Institute for Drug Outcomes Research, NL; Norwegian Health Registries, NHR NO; EpiChron Research Group on Chronic Diseases at the Aragon Health Sciences Institute, ES; Sistema d'Informació per el Desenvolupament de la Investigació en Atenció Primària SIDIAP, ES.

Subjects and study size, including dropouts
The source population was all individuals registered in the health care data sources listed above. Data were extracted from:

- ARS between 27 December 2020 and 31 December 2021
- Pedianet between 31 May 2021and 28 February 2022
- PHARMO between 1 March 2021 and 31 December 2021
- NHR between 01 January 2021 and 31 December 2021
- EpiChron between 27 December 2020 and 31 January 2022
- SIDIAP between 1 January 2021 and 30 December 2021

Variables and data sources:
Exposure was based on recorded prescription, dispensing, or administration of the Pfizer-BioNTech COVID-19 vaccine. Outcomes were identified in the databases with algorithms based on codes for diagnoses. AESIs for inclusion in the study were selected from those proposed by the ACCESS project (http://www.encepp.eu/encepp/viewResource.htm?id=37274).

Results:
A total of 10,347,348 individuals who had received ≥1 dose of Pfizer-BioNTech COVID-19 vaccine and met the inclusion criteria were included in the non-matched vaccinated cohort. Participants were from Italy (ARS 18.7%; PEDIANET <0.1%), the Netherlands (PHARMO 9.8%), Spain (EpiChron 7.1%; SIDIAP 30.0%), and the Norway (NHR 34.3%). A total of 8,641,085 individuals received a second dose, 2,551,466 a third dose, and 3,220 a fourth dose of the Pfizer-BioNTech COVID-19 vaccine. 10,152,493 (98.1%) vaccinated individuals were matched with an unvaccinated individual.

These results provide characteristics and incidence rates of 35 AESIs in more than 10 million vaccinated individuals and more than 10 million unvaccinated controls. Incidence rates of most AESIs were low in the risk interval analysed, and were comparable with prior studies. No systematic or homogeneous differences in the incidence rates were observed between the vaccinated and unvaccinated cohorts.

Discussion:
In this second interim report, we have used all the planned matching criteria (except socio-economic status). Importantly, we also matched on pregnancy status. We verified the balance between matched vaccinated and non-vaccinated individuals. We used a negative control outcome (COVID-19 disease during the first 12 days after time zero) to check if there was residual confounding and if there would be a need to adjust the estimates using weights based on the propensity score. We did not observe an imbalance in the negative control outcome between the matched cohorts and considered matching as adequate. For this second data extraction we included extraction, transformation and harmonization of outcomes and also covariates. Full harmonization of all covariates is ongoing and will be improved for the next interim report. These results should still be considered as preliminary results from a long-term safety surveillance study.

Marketing Authorization Holder(s): BioNTech Manufacturing GmbH, Germany

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