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Safety monitoring of COVID-19 vaccines in multiple European countries: initial results from the COVID-19 Vaccine Monitor (CVM)

Background and objective

The roll-out of the novel COVID-19 vaccines in a large population across multiple countries called for comprehensive monitoring of the safety of these vaccines. The multi-country implementation of a cohort event monitoring study with a common protocol and pooled data shared in real-time provides additional monitoring.

Objective: To report real-time incidence rates of adverse events following immunization (AEFI), serious adverse reactions, and adverse events of special interest (AESI) after receiving one or more EMA-approved COVID-19 vaccines doses.

Method

A prospective cohort event monitoring study was conducted in 13 European countries with four data-collection tools (SafeVac 2.0 platform, web-application OPeN, Lareb Intensive Monitoring (LIM), Research Online (RO) platform) to monitor the safety of first, second, and booster doses of EMA-approved COVID-19 vaccines in both the general population and clinical subgroups of special interest (children/adolescents, pregnant, lactating, immunocompromised, prior SARS-CoV2 infection and allergy). Participants can be included in more than one subset. Participants registered online within two days of receiving the vaccine and reported demographic data, medical history, and AEFI up to six months after vaccination. Incidence rates were calculated for all AEFI after the first and second dose for the general population and for the first booster in the population of special interest.

Results

A total of 642,632 first vaccinated persons have been included after the first dose across 13 countries. Germany included the large majority of vaccinees (n=612,078, 95.2%) through the SafeVac 2.0 platform. Through the LIM data collection tool, a total of 29,846 persons (4.6%) have been included from 5 countries. A total of 3,142 (0.49%, 95%CI: 0.47-0.51%) of the 642,632 vaccinated persons reported at least one serious adverse reaction after receiving the first dose.

Of the 642,290 participants who had received a first dose of any COVID-19 vaccine, 466010 (72.6%) provided follow-up data after dose 2. Of these participants, 495383 (77.1%) and 381876 (81.9%) reported experiencing at least one adverse reaction after dose 1 and 2.

Injection site pain (57.8%, n=371,526) was the most commonly reported, solicited ADR, for each vaccine and both doses. Fatigue, headache, malaise, and myalgia were the most frequently reported solicited systemic adverse reactions (≥20%).

Of the 642,290 participants who had received a first dose of any COVID-19 vaccine, 0.31% (95%CI 0.30-0.33%) subjects reported experiencing at least one AESI between their first and second dose of the vaccine.

Figure 1 shows a heatmap of the percentages of participants who reported any suspected adverse reaction for the 1st and 2nd doses across vaccine brands and age groups and stratified by sex, based on a subset of the total population consisting of LIM App using countries who included subjects at first vaccination. This shows that reactions were more frequent after first than second dose of AstraZeneca, across all strata and after second dose for Moderna. Older people report less ADRs, across all vaccines and females report more frequently than men.

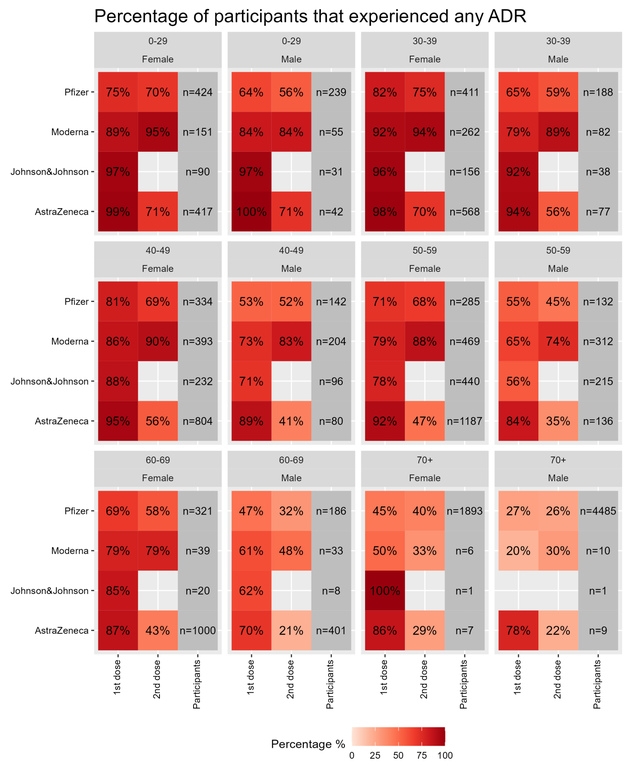

Figure 1. Heatmap for any ADR in total population recruited at first vaccination excluding Germany and Croatia

First vaccination cycle in special populations

A total of 7,503 vaccinees (excluding vaccinees from Croatia) belonging to a special cohort (children and adolescents, immunocompromised, people with history of allergy, people with prior SARS-CoV-2 infection and pregnant women) were included at first vaccination cycle through either LIM or RO.

Serious ADR rates were 0.2% (95%CI: 0.1-0.4%) in people with prior SARS-CoV-2 infection, 0.2% (95%CI: 0.1-0.4%) in people with history of allergy, 0.5% (95%CI: 0.1-1.5%) in immunocompromised, 0.3% (95%CI: 0.1-1.0%) in children/adolescents and 0.6% (95%CI 0.1-3.2%) in pregnant women.

As for the AESI rates, 0.1% (95%CI: 0.0-0.3%) in people with prior SARS-CoV-2 infection, 0.4% (95%CI: 0.3-0.7%) in people with history of allergy, 0.2% (95%CI: 0.0-1.0%) in immunocompromised were observed. Overall, more than half of the vaccinees in each cohort reported at least one ADR (solicited or unsolicited) following the first dose of any vaccine.

Conclusions

While a majority of the participants reported experiencing at least one AEFI after vaccination, only a small proportion was considered an AESI or serious event. This is in line with the data reported from clinical trials and other cohort event monitoring studies. A common data model has been developed for further analysis of reported events, comparisons between groups, and confounding.

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Conflicts of interest/Competing interests

Nicolas Thurin and Caroline Dureau-Pournin work for Bordeaux PharmacoEpi, an independent research platform of the Bordeaux University and its subsidiary the ADERA, which performs financially supported studies for public and private partners, in compliance with the ENCePP Code of Conduct. Miriam Sturkenboom and Sandor Schmikli work for the University Medical Center Utrecht, which performs COVID-19 vaccine trials and post-licensure vaccine effectiveness and safety studies for public and private organisations, according to ENCePP code of conduct of scientific independence. Gianluca Trifirò reported to advisory boards on topics not related to this presentation and was sponsored by the following pharmaceutical companies in the last two years: Eli Lilly, Sanofi, Amgen, Novo Nordisk, Sobi, Gilead, Celgene, Daikii Sankyo.

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