COVID-19

CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION AGAINST COVID-19 AND OTHER UPDATES

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OFFICIAL REPORTS ON PHARMACOVIGILANCE PROGRAMS

ARGENTINA

- As of 3 February 2021, 436,269 vaccine doses have been administered (Sputnik V).
- 16,455 adverse events following immunization (AEFI) (3.8%) were reported, with 0.5% (84) hospitalized for supportive care. The hospitalized patients recovered.
- The most common events reported are: fever with headaches and/or muscle pain; headaches and/or muscle pain; local pain and/or local reaction and/or local tingling or prickling sensations.

Link: https://bancos.salud.gob.ar/recurso/sexto-informe-de-seguridad-en-vacunas

BRAZIL

- A report from the ANVISA pharmacovigilance notifications website on 15 February indicated 452 adverse events resulting from Coronavac (Sinovac) and ChAdOx1 nCoV-19 (Oxford-AstraZeneca); 17.9% were classified as severe, 44.3% non-severe, and 37.6% did not have additional information.
- Most of the cases were headaches, fever, fatigue, and muscle pain.
- 19 fatal cases were reported. However, there is no evaluation report available from the agency regarding these cases.

Link: http://portalanalitico.anvisa.gov.br/vigimed

CANADA

- As of 5 February 2021, 1,042,171 doses of Pfizer-BioNTech and Moderna vaccines had been administered.
- 651 AEFI (0.053% of administered doses) were reported. Of these, 99 (0.009%) were considered severe, with anaphylaxis the most frequently reported event.
- The most reported adverse events were injection site reactions, tingling or prickling sensations, itching, hives, headache, numbness, nausea, and anaphylaxis.
- Most of the reported events involved women.
- In total, there were six adverse events in which death was reported after vaccine administration. Medical review determined that these deaths were not linked to the COVID-19 vaccine.

Link: https://health-infobase.canada.ca/covid-19/vaccine-safety/

CHILE

- Between 24 December 2020 and 20 January 2021, 61,690 doses of the Pfizer-BioNTech SARS-CoV-2 vaccine were administered.

- 847 AEFI were reported (1.4% of administered doses), 661 of them in women (78.5%).
- Severe AEFI accounted for 1.7% of reports. No fatal cases associated with vaccination were reported.
- The most reported adverse events were injection site pain, headache, fever, muscle pain, and general pain.

Link: https://www.ispch.cl/wp-content/uploads/2021/02/20210212-Segundo-Informe-Estad%C3%ADstico-VF-jrs-1.pdf

MEXICO

- As of 15 February 2021, 749,682 doses of the Pfizer-BioNTech vaccine had been administered.
- 6,691 AEFI (0.9% of administered doses) were reported, with 6,658 non-severe and 33 severe cases (25 women and 8 men). Of these, 31 were discharged and 2 remain hospitalized.

Link: https://www.youtube.com/watch?v=JWkJVXNMuuM

SPAIN

- As of 24 January, 1,131,805 people had been vaccinated in Spain; 1,046,629 people received 1,112,982 doses of the Pfizer-BioNTech vaccine (66,353 received both doses); 18,823 doses of the Moderna vaccine were also administered.
- 1,537 adverse events were reported for the Pfizer-BioNTech vaccine (138/100,000 doses) and 18 for the Moderna vaccine (96/100,000 doses).
- The most common events reported for the Pfizer-BioNTech vaccine included fever or pain at the injection site, and nervous system (mostly headaches and dizziness) and gastrointestinal symptoms (primarily nausea and diarrhea). Moderna vaccine: fever or injection site pain, and nervous system (primarily headaches and dizziness) and musculoskeletal system symptoms (mostly pain in the limb where the vaccine was administered and joint pain).
- Most cases were reported in women (81% for Pfizer-BioNTech and 94% for Moderna) and in people between 18 and 64 years old (67%).
- 8 cases of anaphylaxis were identified in the period covered in this report, only for the Pfizer-BioNTech vaccine.

Link: https://www.aemps.gob.es/informa/boletines-aemps/boletin-fv/2021-boletin-fv/2o-informe-de-farmacovigilancia-sobre-vacunas-covid-19/?lang=en

UNITED STATES

- Nearly 41 million doses of the Pfizer-BioNTech and Moderna vaccines were administered between December 2020 and 7 February 2021.

- The Vaccine Adverse Event Reporting System (VAERS) received 1,170 reports of death (0.003%) among those vaccinated. Analysis revealed no link between these deaths and vaccination.
- Anaphylaxis is a rare event that occurs in 2 to 5 people per million vaccinated. It happens about 30 minutes after vaccination and can be treated effectively and immediately.

Link: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html

VigiBase results

VigiBase is the World Health Organization (WHO) global database of individual safety case reports (ICSRs). It is the largest such base in the world and has been administered by the WHO Collaborating Centre for International Drug Monitoring since 1968.

As of 7 February 2021, 67,277 cases had been reported, of which 1,227 were fatal. Of these cases, 51,701 occurred in women and 13,928 in men. Fatal cases occurred at a higher rate in men and in patients over the age of 75 than in women; 625 fatal cases were women and 589 were men, indicating a higher adverse event mortality rate for men. People over the age of 75 are the age group with the highest adverse event fatality rate.

The ten countries contributing the most AEFI to the database were: the United Kingdom (28,211; 41.9%); United States (11,638; 17.3%); Italy (10,736; 16.0%); Spain (3,348; 5.0%); Germany (2,237; 3.3%); Netherlands (1,966; 2.9%); France (1,541; 2.3%); Portugal (1,043; 1.6%); Denmark (786; 1.2%); and Greece (590; 0.9%).

Fatal cases: United States (551; 44.9%); United Kingdom (213; 17.4%); Germany (127; 10.4%); France (65; 5.3%); Norway (58; 4.7%); Sweden (58; 4.7%); Belgium (21; 1.7%); Spain (21; 1.7%); Austria (17; 1.4%); and Italy (15; 1.2%).

The main AEFI reported were: headache (28.3%); fever (23.1%); fatigue (16.4%); muscle pain (14.4%); chills (13.9%); nausea (13.4%); injection site pain (8.5%); joint pain (8.4%); dizziness (8.0%); and pain in the limbs (7.5%).

Safety updates from the European Medicines Agency (EMA) on the Pfizer-BioNTech and Moderna vaccines

The Pharmacovigilance Risk Assessment Committee (PRAC) presented the first updated vaccine safety reports authorized by the EMA, stating the following:

- Anaphylaxis is a known effect of the Comirnaty vaccine (Pfizer-BioNTech) and no additional developments about this event have been identified to date.
- In the United States, the rate of this event is 11 cases per million, however, further analysis is required to determine the frequency in the European Union.

- Reports of death in frail older adults do not suggest Comirnaty safety issues, according to PRAC analysis. In many people over the age of 65, multiple pre-existing comorbidities appear to be the probable cause of death. Therefore, no amendments were required to the product use information, including indications for use in this population.
- Anaphylaxis after administration of the Moderna vaccine occurred at a rate of 2.5 cases per million doses according to case information in the United States. Consequently, PRAC did not identify a safety problem, but requested the manufacturer to continue monitoring and evaluating this event.
- The most common adverse events associated with the two analyzed vaccines are mild or moderate and usually improve a few days after vaccination.

Links:

https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-comirnaty-january-2021_en.pdf

https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-covid-19-vaccine-moderna-february-2021_en.pdf

NEW STUDIES AND DEVELOPMENTS

The CanSino COVID-19 vaccine shows 65.7% effectiveness (02/08)

In a phase 3 study, the CanSino Biologics viral vector vaccine produced in China shows 65.7% effectiveness in preventing symptomatic illness. According to results in Pakistan, the vaccine is 90.98% effective in preventing severe illness. It is important to note that, like the Johnson & Johnson vaccine, this is a single-dose vaccine. Both vaccines have the advantage of being single-dose and are more easily stored than mRNA vaccines. The phase 3 study included 30,000 participants from Pakistan, Russia, Argentina, Mexico, and Chile.

Source: China's CanSino Covid Vaccine Shows 65.7% Efficacy. Bloomberg. 8 February 2021.

IMPACT OF NEW SARS-CoV-2 VIRUS VARIANTS

The coronavirus variants that have appeared in the United Kingdom (B.1.1.7) and South Africa (B.1.351) have been associated with increased virus transmissibility. Some of the variants contain mutations of the coronavirus' spike protein, which in principle could affect the ability of antibodies to bind to and neutralize the virus.

Moderna has tested blood samples from patients vaccinated with their mRNA vaccine to analyze their ability to neutralize the B.1.1.7 and B.1.351 variants (pseudovirus neutralization). The tests have shown the same neutralization levels for B.1.1.7. Neutralization levels for B.1.351 levels are decreased but remain above the protective levels identified in non-human primate studies. One option could be to administer of a third dose of vaccine to ensure maintained immunity over a longer period.

Source: Kai Wu, Anne P. Werner, John I. Moliva, Matthew Koch, et al. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. doi: https://doi.org/10 125.1101/2021.48.4279

South Africa: SARS-CoV-2 variants

Initial trials in South Africa with the Oxford-AstraZeneca vaccine indicate "minimum protection" against mild COVID-19 due to variants 501.V2 or B.1.351. This study, currently pending publication, involved 2,000 people with an average age of 31 years. In any case, researchers assume, even without confirmation from specific studies, that the vaccine should protect against severe COVID-19. Work will begin developing a modified vaccine by autumn to combat the South African variant. South Africa has halted use of the vaccine while scientists advise on how best to proceed after obtaining results from the study. Also known as 501.V2 or B.1.351, it is already the dominant virus variant in large parts of South Africa.

Based upon the above information, South Africa has decided to start vaccinating frontline health workers with the still unapproved Johnson & Johnson vaccine. This initiative will be used to study the effectiveness of this strategy,

particularly against a variant that has become dominant in the country. Meanwhile, South Africa's regulatory authority will continue the vaccine approval process.

Sources:
Oxford Covid-19 vaccine trial results. University of The Witwatersrand, Johannesburg. 7 February 2021.

Madhi SA, Baillie V, Cutland CL, Voysey M, et al. Safety and efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine against the B.1.351 variant in South Africa. doi: https://doi.org/10.1101/2021.210.21251247

COVID-19 tracker: BD's new combo COVID test IDs virus variants, too; FDA's pandemic inspection backlog grows. Fierce Pharma. 12 February 2021.

Bell's Palsy study (facial paralysis)

As of 31 January 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) has received 99 reports of facial paralysis or muscle weakness with the Pfizer-BioNTech vaccine. This event is currently indicated as a possible side effect of the Pfizer-BioNTech vaccine based on a small number of reports in clinical trials. However, no association with the vaccine has been confirmed, as this effect can also occur naturally. Fifteen reports of facial paralysis have been received for the Oxford/AstraZeneca COVID-19 vaccine.

In addition to individual clinical review of these reported events, analysis is under way based on expected occurrence in the absence of vaccination (the "natural rate"). Review has shown that reports of facial paralysis indicate similarity to the expected natural rate, which does not currently suggest increased risk after vaccination. These events will continue to be monitored, including evaluation of electronic health care log data.

Link: https://bit.ly/2ZmyOAQ

Immune thrombocytopenia

According to the New York Times, there are 36 reports of people who developed immune thrombocytopenia, a rare blood disorder, soon after receiving the Pfizer or Moderna vaccine. Officials from the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) are investigating and have indicated that these cases could be coincidental and unrelated to the vaccines used. In clinical trials, involving approximately 30,000 and 44,000 people (Moderna and Pfizer-BioNTech respectively), no immune thrombocytopenia events were reported. According to the FDA, approximately 1 in 35,000 people are reported to have this condition per year in the United States.

Sources:
A Few Covid Vaccine Recipients Developed a Rare Blood Disorder. The New York Times. 8 February 2021.

A Small Number of People Developed This Rare Blood Disorder After Getting a COVID Vaccine—Here's What to Know. Explore Health. 10 February 2021.

Impact of a vaccine dose on people previously infected with COVID-19

A recently published study on the impact of a dose of BNT162b2 mRNA COVID-19 vaccine shows immunogenicity in a vast majority of the study population (92%) 21 days after vaccination. It should be noted that the study population is small and did not allow for the analysis to be adjusted. The results also show that vaccination was a "boost" for individuals with proven prior COVID-19 infection, and antibody titer amounts were greater than in individuals without prior infection. It is interesting to note that this response was proven regardless of whether the individual had detectable antibodies against SARS-CoV2 N (nucleocapsid protein) before vaccination. Although the observations were made only in 17 individuals, they provide confidence that the rapid decrease of antibodies against the nucleocapsid protein after infection does not necessarily mean loss of immunity, and that B cells immune memory is maintained regardless of IgG levels.

Source: Kamal AJ, Hila BA, Karine B, Yunis B, et al. Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021. EuroSurveill. 2021;26(6):p ii-2100096. https://doi.org/10.2807/1560-7917.ES.2021.26.6.2100096

CONCLUSIONS OF EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

Currently, there are no additional updates other than those in the last shared note on conclusive analyses of AEFI.

PROGRAMMATIC ERRORS, LOGISTICS, AND RELATED ISSUES

Moderna and 15 doses

Moderna has asked the FDA for authorization to fill its COVID-19 vaccine vials with five additional doses to ease a bottleneck in manufacturing. The change would allow Moderna to put 15 doses in vials of the same size currently authorized to contain 10, alleviating pressure during the filling process. Recently, the FDA authorized Moderna to put up to 40% more coronavirus vaccine in each vial, increasing the amount from 10 to 14 doses per vial.

Source: F.D.A. Agrees Moderna Can Increase Vaccine Supply in Each Vial. The New York Times. 12 February 2021.

Japan: The importance of low-dead-space syringes

After securing the purchase of 144 million doses of the Pfizer-BioNTech vaccine for 72 million people, Japan's health minister noted that, due to lack of low-dead-space syringes needed to extract a sixth dose from vials, some 24 million doses of vaccines would be wasted.

Source: Fewer people in Japan to get Pfizer vaccine due to syringe shortage. The Japan Times. 10 February 2021.

Second dose of Moderna and Pfizer vaccines

The CDC continues to recommend that people receive their second dose of the COVID-19 vaccine as close as possible to the recommended interval (3 weeks for Pfizer-BioNTech, and one month for Moderna). The CDC guidelines were updated to allow administration of the second dose up to 6 weeks (42 days) after the first dose if it is not feasible to stick to the recommended interval. The CDC does not advocate delaying the second dose, but clinical trial data support this range.

In exceptional circumstances, for example when the first dose vaccine product cannot be determined, the CDC updated its guidelines to allow administration of any available mRNA COVID-19 vaccine to complete the COVID-19 mRNA vaccination series, with a minimum interval of 28 days between doses. COVID-19 vaccines are not interchangeable. In extremely rare situations, some people may simply lack documentation or not know which vaccine they got for their first dose.

Link: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Argentina: Update on special situations in the target population to be vaccinated (persons who are pregnant, breastfeeding, immunocompromised, or have autoimmune diseases)

The National Immunization Commission (Comisión Nacional de Inmunizaciones, CoNaIn)—in consensus with various scientific societies and experts outside the National Ministry of Health (Ministerio de Salud de la Nación), and in accordance with analyses and recommendations published in recent weeks in other countries—has recommended to the Ministry of Health that persons who are part of the target population to be vaccinated but who are pregnant, breastfeeding, or immunocompromised, or who have autoimmune diseases should be excluded from the category "contraindicated for vaccination against COVID-19" (provided that the vaccines are NOT live and attenuated viruses). (02/11)

Source: Sputnik V: update on special situations in the target population to be vaccinated (persons who are pregnant, breastfeeding, immunocompromised, or have autoimmune diseases). Femeba Foundation. 10 February 2021

COVID-19 vaccine delivery by drone

Zipline Inc., which delivers medical supplies by drone, plans to begin delivering COVID-19 vaccines in April 2021 in partnership with an unknown vaccine manufacturer. The system can distribute vaccines that require ultra-low temperatures in geographically hard to reach locations without the need for freezing in intermediary centers. The company has been using drones to deliver medical supplies to rural areas in Rwanda and Ghana since 2016, and in 2020 delivered personal protective equipment in North Carolina.

Source: Medical Drone Startup to Begin Covid Vaccine Delivery in April. 02/04/2021.