COVID-19

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

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OFFICIAL REPORTS ON PHARMACOVIGILANCE PROGRAMS

ARGENTINA

- As of 11 February 2021, 572,928 doses of the Sputnik V vaccine had been administered.
- 19,014 adverse events following immunization (AEFI) (3.3%) were reported; of these, 106 (0.55%) were hospitalized for symptomatic treatment and subsequently recovered.
- The most common events reported are: fever with headache and/or muscle pain; headache and/or muscle pain; local pain and/or local reaction and/or local tingling or prickling sensations.

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

CANADA

- As of 12 February 2021, 1,221,539 doses of the Pfizer-BioNTech and Moderna vaccines had been administered.
- 957 AEFI (0.078% of administered doses) were reported. Of these, 140 (0.011%) were considered severe, with anaphylaxis as the most frequently reported event.
- Injection site reactions, tingling or prickling sensations, itching, hives, headache, numbness, nausea, and anaphylaxis accounted for 62% of mild to moderate events reported.
- 50% of events were reported in women between the ages of 18 and 49.
- A total of eight reported adverse events involved post-vaccine death. Medical review determined that five of these deaths were not linked to administration of the COVID-19 vaccine. The other three are still under investigation.

Link: https://www.canada.ca/en/public-health/news/2021/02/statement-from-the-chief-public-health-officer-of-canada-on-february-22-2021.html

COLOMBIA

- Although uncorroborated on official INVIMA and Ministry of Health websites, some media outlets reported five suspected cases of serious adverse event after vaccination in Bogota during the second day of vaccination in Colombia, according to information from the National Institute of Health on 18 February 2021.
- Four women and one man, 25 to 41 years of age, had symptoms such as vertigo, itching, palpitations, nausea, and low blood pressure after receiving a dose of the Pfizer vaccine.
- These patients received medical treatment and are stable. The situation is being monitored by local and national health authorities.
- This information needs to be confirmed by official sources in future updates.

COSTA RICA

- As of 12 February 2021, the Directorate of Epidemiological Surveillance of the Costa Rican Social Security Fund reported that a total of 96,948 people had been vaccinated against COVID-19; 56% (n = 54,395) received the first dose and the remaining 44% received the second dose (n = 42,553).
- From 24 December 2020 to 12 February 2021, the National Pharmacovigilance Center (known in Spanish as CNFV) analyzed 830 AEFI reports associated with the Pfizer-BioNTech COVID-19 vaccine. Reports come mostly from health professionals.
- During the week of 5 to 12 February, 362 AEFI were reported; 70% occurred in women and 41% in people from 30 to 39 years of age.
- 100% of AEFI analyzed were classified as non-severe and 95% as mild. The most common events were central nervous system (headache) and injection site symptoms (local or injection site pain).
- No cases of anaphylaxis were reported during this period. However, the CNFV is constantly monitoring for this type of AEFI.

Source: Report of adverse events following immunization (AEFI) with the Pfizer-BioNtech COVID-19 vaccine from 5 to 12 February 2021. Directorate for Regulation of Health Products National Pharmacovigilance Center (CNFV), Ministry of Health of Costa Rica.

FRANCE

- Vaccine surveillance updates from 5 to 11 February show 3,634 analyzed adverse events from the Pfizer-BioNTech Comirnaty vaccine. Most of them were expected and non-severe.
- New cases of high blood pressure (55 severe cases) and cardiac arrhythmia (42 severe cases), mostly transient and reversible, were confirmed for this vaccine, without calling into question its risk/benefit ratio.
- 87 cases associated with the Moderna vaccine have been analyzed, mostly non-severe delayed local reactions. These events do not raise safety concerns.
- Symptoms similar to flu syndrome reported among health professionals who received the AstraZeneca vaccine on 11 February are being monitored; 363 professionals (average age = 31 years) with high fever, body aches, and headaches were analyzed. No concerns were raised about the vaccine's risk/benefit ratio.
- The National Agency for Medicines and Health Products Safety recommended that health workers continue receiving vaccinations in health facilities on a staggered schedule to avoid potential service disruptions. Sweden and Germany have identified the same events. They are being evaluated at the European level.

Source: https://ansm.sante.fr/S-informer/Actualite/Point-de-situation-sur-la-surveillance-des-vaccins-contre-la-COVID-19

MEXICO

- As of 23 February 2021, 1,801,156 doses had been administered: 940,706 doses of Pfizer-BioNTech vaccine, and 860,450 doses of AstraZeneca vaccine.
- 8,109 AEFI were reported (0.5% of all doses administered), 8,060 of them non-severe and 49 severe. Of the latter, 41 had received the Pfizer-BioNTech vaccine, and eight had received AstraZeneca (38 women and 11 men); 36 were discharged and 13 remain hospitalized; 7,884 adverse events were reported for the Pfizer-BioNTech vaccine and 225 for AstraZeneca.

Link: https://www.gob.mx/salud/prensa/version-estenografica-conferencia-de-prensa-informe-diario-sobre-coronavirus-covid-19-en-mexico-264751?idiom=es

NEW STUDIES AND DEVELOPMENTS

Pfizer-BioNTech will begin global clinical trials to evaluate its COVID-19 vaccine in pregnant women

This will be a Phase 2/3, randomized, placebo-controlled, observer-blind study of approximately 4,000 healthy pregnant women 18 years of age or older, who were vaccinated at 24 to 34 weeks gestation. The safety, tolerability, and immunogenicity of BNT162b2 vaccine or placebo, administered 21 days apart, will be evaluated. Safety and the transfer of protective antibodies in newborns of vaccinated pregnant women will be monitored. Newborns will be monitored for six months. Previous DART (developmental and reproductive toxicity) studies showed no evidence of fertility or reproductive toxicity in animals.

Source: Study to Evaluate the Safety, Tolerability, and Immunogenicity of SARS CoV-2 RNA Vaccine Candidate (BNT162b2) Against COVID-19 in Healthy Pregnant Women 18 Years of Age and Older - Full Text View - ClinicalTrials.gov

Spread of SARS-CoV-2 and the Pfizer-BioNTech vaccine

The Pfizer-BioNTech vaccine appears to stop the vast majority of recipients in Israel becoming infected, which could indicate that it curbs transmission of the virus. The vaccine was 89.4% effective at preventing laboratory-confirmed infections, according to unofficial information. If confirmed, early laboratory results may indicate that the vaccine also prevents asymptomatic carriers from spreading the virus that causes COVID-19. Developers are analyzing the data obtained in Israel but the information is not yet ready for publication.

Source: Pfizer-BioNTech Shot Stops Covid Spread, Israeli Study Shows. 21 February 2021

IMPACT OF NEW SARS-CoV-2 VIRUS VARIANTS

Evolution of the SARS-CoV-2 virus, impact of circulating variants, and new vaccines

Ester Lázaro, director of the group working on "Experimental evolution with viruses and microorganisms" at the Center for Astrobiology (CSIC-INTA) in Madrid[1] (an institution affiliated with NASA's Astrobiology Institute), explained how the SARS-CoV-2 virus has evolved and implications for the emergence of new variants. Selected highlights are described below.

Coronaviruses have less capacity for mutation than other RNA viruses, as they have a mechanism that corrects some of the errors that occur during genome copying in virus replication. However, this does not prevent coronaviruses from constant random mutations. This explains why viruses isolated from different patients show some differences. However, these differences by and large do not represent any major changes in the behavior of the virus; mass

[1] Center for Astrobiology (CSIC-INTA) in Madrid, cab.inta-csic.es

spread in the population is not due to mutation, but rather because these viruses are easily transmitted by individuals with many contacts or who travel frequently.

Less frequently, mutations occur that have advantages over the original virus. However, as the number of people who have been vaccinated or who have recovered from infection increase, so does the number of individuals with antibodies to the COVID-19 virus. This, coupled with measures to curb contagion, (use of masks, ventilated spaces, social distancing, etc.) impedes transmission. Thus, it is to be expected that the predominant variants will bypass recognition by the immune system or interact more easily with the cell receptor and manage to infect it.

This is being observed with the new variants of SARS-CoV-2 (British, South African and Brazilian). Each variant contains a particular set of S or "spike" protein mutations, which leads to greater transmissibility and, in the case of the South African variant, the ability to evade the immune response generated by prior contact with the virus or by vaccination.

The N501Y mutation is characterized by an increased ability to bind to the cell receptor (the ACE2 protein), leading to greater transmissibility. This mutation is found in all three variants (British, South African, and Brazilian). Also, the E484K mutation, present in the South African variant, evades the immune response. This means the virus may not be recognized by antibodies generated by previous infections or by the vaccine.

New variants are expected to continue appearing. As a result, studies are underway to determine the three-dimensional structure of the virus' proteins and potential modifications after mutation. These studies seek to predict the impact on virus entry into the cell in order to generate new strategies to develop or modify COVID-19 vaccines.

Source: Ester Lázaro: "We must pay attention to how the virus evolves, without sounding the alarm". Genotipia. 16 February 2021

New strategies to reduce SARS-CoV-2 infection and viral transmission

Researchers from different institutions in the United States, Italy, and the Netherlands have developed a possible intranasal prophylactic treatment, based on lipopeptide inhibitors of fusion between viral and host cell membranes, a critical stage in SARS-CoV-2 infection.

Based on the results obtained from in vitro efficacy and in vivo biodistribution of lipopolypeptides, a dimeric form was selected for evaluation in an animal model. Daily intranasal administration to ferrets completely prevented SARS-CoV-2 direct-contact transmission during 24-hour co-housing with infected animals, under stringent conditions that resulted in infection of 100% of untreated animals.

According to the researchers, these lipopeptides are highly stable and thus may readily translate into safe and effective intranasal prophylaxis to reduce transmission of SARS-CoV-2.

Source: Intranasal fusion inhibitory lipopeptide prevents direct-contact SARS-CoV-2 transmission in ferrets. Rory D. de Vries1, Katharina S. Schmitz, Francesca T. Bovier, Camilla Predella, Jonathan Khao, Danny Noack, Bart L.

Haagmans, Sander Herfst, Kyle N. Stearns, Jennifer Drew-Bear, Sudipta Biswas, Barry Rockx, Gael McGill, N. Valerio Dorrello, Samuel H. Gellman, Christopher A. Alabi, Rik L. by Swart, Anne Moscona, Matteo Porotto. Science 17 Feb 2021: eabf4896. DOI: 10.1126/science.abf4896

The Oxford/AstraZeneca vaccine is more effective with a longer interval between doses

A study published in The Lancet shows that the vaccine developed by AstraZeneca and Oxford University against COVID-19 has improved effectiveness if the second dose is given three months after the first dose, rather than six weeks. The study confirmed AstraZeneca's findings in early February, showing 76% effectiveness against symptomatic coronavirus infection for three months after the first inoculation. The duration of protection with a single dose has not been determined, as no follow-up has been conducted for longer periods; 81% effectiveness was shown when the second dose is administered after 12 weeks, compared to 55.1% with a 6-week interval. According to the study, greater protective efficacy associated with a stronger immune response is achieved with a longer interval between doses.

Although the second dose is considered important to ensure long-term immunity, deferring the second dose to three months would increase the number of people vaccinated with at least one dose of the vaccine.

Sources:

Voysey M, Clemens SAC, Madhi SA, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. Lancet 2021; published online Feb 19.

Voysey M, Costa Clemens SA, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021; 397: 99–111.

3 CLARIFICATIONS/CONCLUSIONS OF EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

Currently, there are no additional updates to those of the last update on conclusive AEFI analyses.

PROGRAMMATIC ERRORS, LOGISTICS, AND RELATED ISSUES

Problems with incorrect dosage amounts

A Massachusetts pharmacy reported an error leading to smaller than recommended doses of COVID-19 vaccine being administered to a limited number of vaccinated people. People received 0.3 ml instead of the recommended 0.5 ml for the vaccine.

Source: CVS gives wrong COVID-19 vaccine dose to patients. WRAL.com. 19 February 2021

Request to change storage conditions

Pfizer-BioNTech submitted new data to the U.S. Food and Drug Administration (FDA) demonstrating the stability of their COVID-19 vaccine when stored at -25°C to -15°C (-13°F to 5°F), temperatures more commonly found in pharmaceutical freezers and refrigerators. The data have been submitted to the FDA to support a proposed update to the U.S. Emergency Use Authorization (EUA) Prescribing Information, which would allow for vaccine vials to be stored at these temperatures for a total of two weeks as an alternative or complement to storage in ultra-low temperature freezers.

Source: Pfizer and BioNtech submit covid-19 vaccine stability data at standard freezer temperature to the U.S. FDA. Pfizer News. 19 February 2021

Inclusion of pregnant and nursing women in COVID-19 vaccine research

The manufacturers of both currently available COVID-19 vaccines, and of many vaccines under development, excluded pregnant and lactating individuals from the clinical trials needed to obtain Emergency Use Authorizations from the FDA. Now that the vaccines are being distributed, the U.S. Centers for Disease Control and Prevention (CDC) and the FDA will obtain information from those who receive them in order to measure their potential impact on women during pregnancy and on infants following birth. While these data will prove very useful, pregnant individuals and their clinicians must make real-time decisions about the vaccine based on little or no scientific evidence that applies specifically to pregnant and lactating individuals.

Source: NIH calls for greater inclusion of pregnant and lactating people in COVID-19 vaccine research. 19 February 2021 https://www.nih.gov/news-events/news-releases/nih-calls-greater-inclusion-pregnant-lactating-people-covid-19-vaccine-research

According to a recent publication in the JAMA academic journal, "the continued global escalation of coronavirus disease 2019 (COVID-19) cases is of particular concern to pregnant and lactating individuals. While many cases of COVID-19 are asymptomatic or relatively mild, recent evidence suggests that pregnant people are at increased risk of hospitalization and have a 3-fold adjusted relative risk of needing intensive care (10.5 vs 3.9/1000 cases) and mechanical ventilation (2.9 vs 1.1/1000 cases) compared with age-matched nonpregnant individuals." With the development of COVID-19 vaccines, there is the potential for prevention of this illness; however, there is no available

evidence for the utility, safety, and effectiveness of the available vaccines in pregnancy. Thoughtfully including pregnant and lactating individuals in clinical research will lead to clinical care recommendations based on solid evidence.

Source: Bianchi DW, Kaeser L, Cernich AN. Involving Pregnant Individuals in Clinical Research on COVID-19 Vaccines. JAMA. Published online 10 February 2021. 2020. doi: 10.1001/jama.2020.1585.