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# EMA, ISTH, WHO and many countries recommend benefit of COVID-19 vaccination outweighs the risks

## Risks of adverse events no higher in people with bleeding disorders

The European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC), following investigation of isolated cases of unusual blood clotting with low blood platelets that have occurred in a small number of cases worldwide, on April 7 reiterated that the benefits of COVID-19 vaccination outweigh the potential risk of adverse reactions.[1]

In recent weeks, there have been reports from several countries suggesting that there is a link between AstraZeneca's COVID-19 vaccination and unusual blood clotting reactions seen in a small number of cases. The European regulatory authority investigated 169 cases of blood clotting in the brain (cerebral venous sinus thrombosis, CVST) and 52 cases in the abdomen (splanchnic vein thrombosis) among 34 million people vaccinated, reported to the EU drug safety database EudraVigilance (as of April 4, 2021).[1]

The April 4 data suggest a risk estimate of 1:153,000 for these thromboembolic events. It is important to note that risk estimates change daily with the increasing numbers of people vaccinated.

Compared to the general population, people with bleeding disorders are not at higher risk of this rare complication and are being advised to take whichever vaccine that is offered to them, in accordance with the vaccine roll-out in their country.

On March 31, the World Health Organization's Strategic Advisory Group of Experts (SAGE) on Immunization stated that AstraZeneca's COVID-19 vaccine is safe and that the evidence still weighs heavily in favour of its use, including in women under age 55, since many of the countries using it have safety warning signal systems in place and are not reporting problems.[2]

On April 9, the International Society of Thrombosis and Haemostasis (ISTH) concurred with the EMA statement.[3] The ISTH added that more rigorous scientific studies need to be undertaken to clearly determine if and how the AstraZeneca vaccine causes these events, and how they can best be diagnosed to be able to recommend the optimal treatments for them.

These rare complications may not be unique to AstraZeneca's vaccine. Very recently several patients who received the Johnson & Johnson COVID-19 vaccine have shown similar complications.[4] Many millions of doses of the Johnson & Johnson vaccine have been administered, so this is also a very rare event. Both vaccines utilize a viral coat (adenovirus) to deliver the SARS-CoV-2 genetic material to initiate immunization.[5,6] Whether these rare adverse events are caused by the adenovirus carrier or the SARS-CoV-2 genetic material remains to be determined.

## Guidance for the management of people with bleeding disorders

The benefits of the vaccine continue to outweigh the risks for people who receive it. The FDA/EMA-approved vaccines are effective at preventing most cases of COVID-19 and greatly reducing, and in some cases eliminating, hospitalizations and deaths among those who have been vaccinated.[1]

The WFH and EHC summarize key points for patients and healthcare professionals, below.

## Information for patients

- Patients are advised to follow their local public health guidelines and get vaccinated as soon as possible.
- The most common side effects are usually mild or moderate and improve within a few days after vaccination.
- Patients should seek medical assistance immediately if they have the following symptoms:
  - shortness of breath
  - chest pain
  - swelling in the leg
  - persistent abdominal (belly) pain
  - neurological symptoms, including severe and persistent headaches or blurred vision
  - tiny blood spots under the skin beyond the site of injection

## Information for healthcare professionals

- These very rare types of thrombosis (with thrombocytopenia) included venous thrombosis in unusual sites such as cerebral venous sinus thrombosis and splanchnic vein thrombosis as well as arterial thrombosis.
- Most of the cases reported so far have occurred in women under the age of 60 years. Most cases occurred within 2 weeks of the person receiving their first dose. There is limited experience with the second dose.
- Healthcare professionals should be alert to the signs and symptoms of thromboembolism and thrombocytopenia. By recognizing the signs of blood clots and low blood platelets and treating them early, healthcare professionals can promptly treat people affected in line with available guidelines, and help them in their recovery and avoid complications.
- Healthcare professionals should tell people receiving vaccines that they must seek medical attention if they show the symptoms of blood clots described above.
- National authorities may provide additional guidance on the roll-out of vaccines based on the situation in their country.

See also the EMA update on the AstraZeneca vaccine and the COVID-19 vaccination guidance for people with bleeding disorders developed by the WFH, EHC, European Association for Haemophilia and Allied Disorders, and U.S. National Hemophilia Foundation.

The WFH and EHC continue to monitor and report on COVID-19 developments which may have impacts on the management of care for people with bleeding disorders.

**References**

1. AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets (EMA, April 7, 2021)

2. WHO: Risk profile for AstraZeneca COVID vaccine "weighs heavily" in favour (Reuters, March 31, 2021)

3. Statement from the ISTH on Reports Indicating Blood Clots Associated With the AstraZeneca Vaccine (ISTH, April 9, 2021)

4. Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 6-9 April 2021 (EMA, April 9, 2021)

5. Schultz NH, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. N Engl J Med April 9, 2021. doi:10.1056/NEJMoa2104882

6. Greinacher A et al. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med April 9, 2021. doi:10.1056/NEJMoa2104840

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