Updated GTH statement following the EMA's decision to continue vaccinations with the AstraZeneca COVID-19 vaccine:

On Friday, March 19, 2021, vaccinations with the COVID-19 vaccine from AstraZeneca will be resumed in Germany. The Paul Ehrlich Institute has now reported more than 13 cases of sinus or cerebral vein thrombosis with> 1.6 million vaccine doses administered by the AstraZeneca company. The thrombosis occurred 4–16 days after vaccination with the AstraZeneca COVID-19 vaccine in twelve women and one man aged 20–63 years. The patients also had thrombocytopenia, which indicates an immunological event as the cause of the tendency to thrombosis.

An important pathomechanism has meanwhile been clarified within the GTH under the leadership of the Greifswald working group around Andreas Greinacher. The vaccination is likely to lead to the formation of antibodies against platelet antigens as part of the inflammatory reaction and immune stimulation. Depending on or independently of heparin, these antibodies then induce massive platelet activation via the Fc receptor in analogy to heparin-induced thrombocytopenia (HIT). This mechanism (HIT mimicry) could be demonstrated in four patients with a sinus / cerebral vein thrombosis after vaccination with the AstraZeneca COVID-19 vaccine in the laboratory of Andreas Greinacher in cooperation with other GTH members. As with classic HIT, these antibodies appear 4–16 days after vaccination. This pathomechanism does not rule out that the sinus / cerebral vein thrombosis after vaccination with the AstraZeneca COVID-19 vaccine also have other causes; However, it forms the basis for the following updated findings and recommendations of the GTH:

• The positive effects of vaccination with the AstraZeneca COVID-19 vaccine outweigh the negative effects, so that the resumption of vaccinations in Germany with this vaccine is to be welcomed. According to the current state of knowledge, there is no evidence that thromboses at typical locations (leg vein thrombosis, pulmonary embolism) are more common after vaccination with the AstraZeneca COVID-19 vaccine than in the age-appropriate normal population.

• Due to the immunological genesis of sinus / cerebral vein thromboses, patients with a positive history of thrombosis and / or known thrombophilia after vaccination with the AstraZeneca COVID-19 vaccine do not have an increased risk of developing this specific and very rare complication.

• Flu-like symptoms such as joint, muscle and headache that persist for 1–2 days after vaccination are a common side effect and are not a cause for concern.

• In the event of side effects that persist or recur> 3 days after vaccination (e.g. dizziness, headache, visual disturbances), further medical diagnostics should be carried out to clarify a cerebral thrombosis.

• Important examinations are in particular the blood count with determination of the platelet count, blood smear, D-dimers and, if necessary, further imaging diagnostics (e.g. cMRI).

• In the event of thrombocytopenia and / or evidence of thrombosis, testing for heparin-induced thrombocytopenia (HIT) should be carried out regardless of previous exposure to heparin. This test is based on the immunological detection of antibodies against the complex of platelet factor 4 (PF4) and heparin.

• Until (autoimmune) HIT has been ruled out, if the clinical situation, availability and experience permit, anticoagulation with heparins should be avoided and alternative, HIT-compatible preparations should be used. An (autoimmune) HIT is formally excluded only if the functional confirmation test (e.g. HIPA) turns out negative.

• In patients with confirmed autoimmune HIT and critical thromboses such as sinus / cerebral vein thrombosis, the prothrombotic pathomechanism can very likely be reduced by the administration of high-dose intravenous immunoglobulins (IVIG), e.g. at a dose of 1 g / kg body weight per day on two consecutive days, to be interrupted.

• Regardless of the cause and the results of a test for PF4 / heparin antibodies, alternative causes of thrombocytopenia and / or thrombosis must be considered and further clarified accordingly. These include, for example, thrombotic microangiopathy (iTTP, aHUS), antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria and underlying malignant (haematological) diseases.

With kind regards

Yours Johannes Oldenburg, Robert Klamroth, Florian Langer, Bernd Pötzsch, Andreas Greinacher