



### **Important note for patients**

We are unable to provide patient counseling and ask that you refrain from inquiring about potential health risks associated with vaccination with the AstraZeneca vaccine. Please contact your treating physician or a coagulation center. Thank you!

Cologne, 03/24/2021

### **Updated GTH statement on vaccination with the AstraZeneca COVID-19 vaccine, as of March 22, 2021**

On Friday, March 19, 2021, vaccinations with the COVID-19 vaccine from AstraZeneca were resumed in Germany. The Paul Ehrlich Institute (PEI) had previously reported on 13 cases of sinus or cerebral vein thrombosis with > 1.6 million AstraZeneca COVID-19 vaccine doses administered. The thromboses 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 classical HIT, these antibodies appear 4–16 days after vaccination. This pathomechanism does not rule out that the sinus / cerebral vein thromboses after vaccination with the AstraZeneca COVID-19 vaccine also have other causes. However, it forms the basis for the following updated statements and recommendations of the GTH:

- On a population basis, 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.

## **GTH**

Gesellschaft  
für Thrombose- und  
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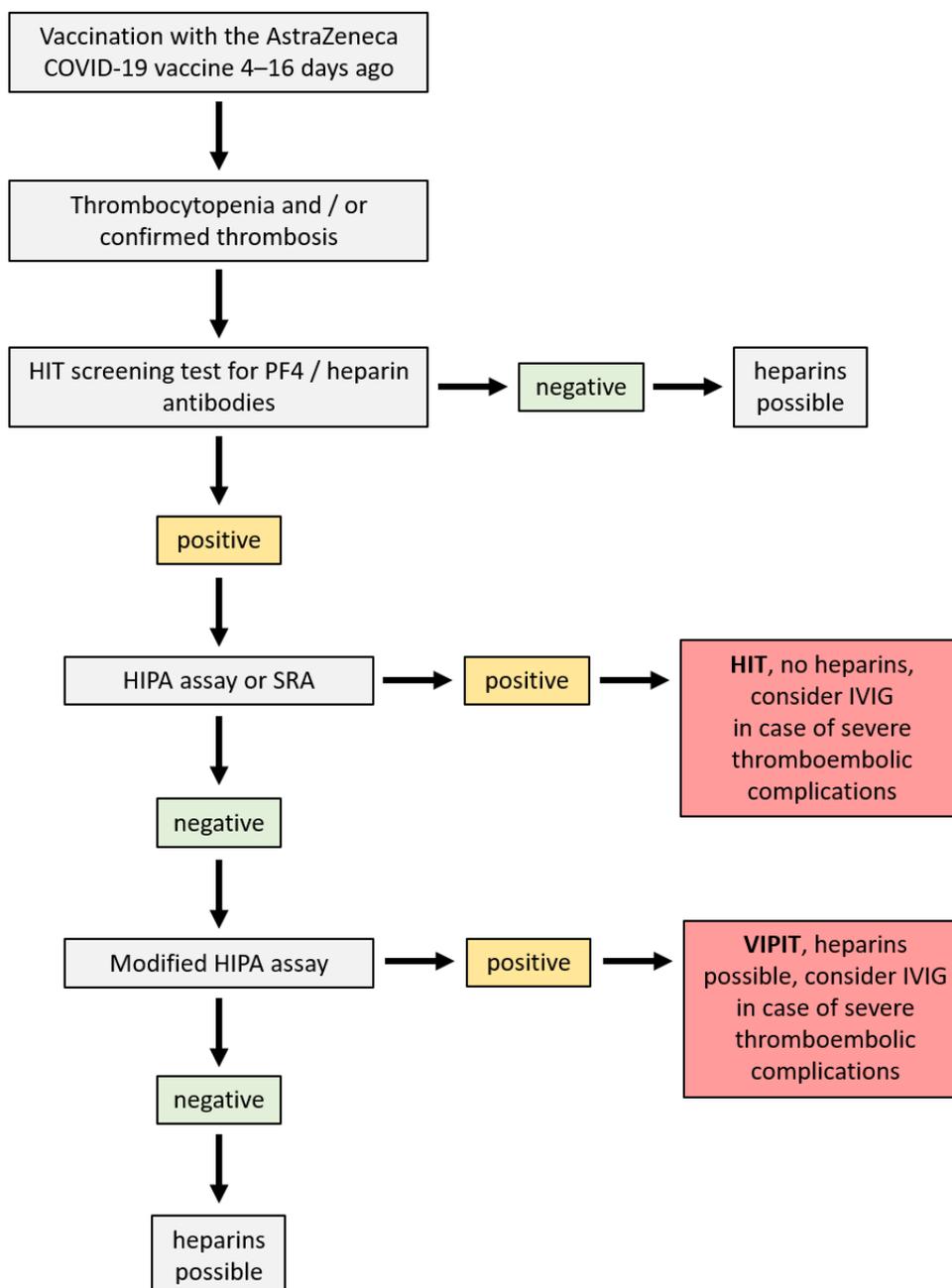
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- According to the current state of knowledge, there is no evidence that thromboses at typical locations (leg vein thrombosis, pulmonary embolism) are more common after vaccination with the AstraZeneca COVID-19 vaccine than in the age-appropriate normal population.
- Due to the immunological genesis of thromboses in intracranial veins or other (atypical) locations, patients with a positive history of thrombosis and / or known thrombophilia do not have an increased risk of developing this specific and very rare complication after vaccination with the AstraZeneca COVID-19 vaccine.
- 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; nausea / vomiting; shortness of breath; acute pain in chest, abdomen, or extremities), further medical diagnostics should be carried out to clarify a 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, ultrasound, CT of chest / abdomen).
- In the event of thrombocytopenia and / or evidence of thrombosis, testing for pathophysiologically relevant antibodies should be carried out regardless of previous exposure to heparin. The first test in the diagnostic algorithm is a screening test for heparin-induced thrombocytopenia (HIT), which is based on the immunological detection of antibodies against the platelet factor 4 (PF4) / heparin complex. In case this test is negative, an HIT-like specific immunological cause of thrombosis / thrombocytopenia can be ruled out. In case this test is positive, a classical HIPA assay (HIPA, heparin-induced platelet activation) or SRA (serotonin-release assay) should be ordered as a functional confirmatory test. These assays detect pathophysiologically relevant antibodies, which activate platelets dependent (typical HIT) or independent of exogenous heparin (autoimmune HIT). A positive test result thus establishes the diagnosis of (autoimmune) HIT. In case the classical HIPA (or SRA) is negative, a modified HIPA assay, which has been established in the laboratory of Andreas Greinacher, Greifswald, should be ordered. This assay detects pathophysiologically relevant antibodies, which show a reaction pattern different from that observed in (autoimmune) HIT. A positive test result thus establishes the diagnosis of vaccine-induced prothrombotic immune thrombocytopenia (VIPIT).
- Until (autoimmune) HIT is ruled out, if the clinical situation, availability and experience permit, anticoagulation with heparins should be avoided and alternative, HIT-compatible anticoagulants should be used.
- In patients with confirmed (autoimmune) HIT or VIPIT and critical thromboses such as sinus / cerebral or splanchnic vein thrombosis, the prothrombotic pathomechanism can very likely be interrupted by the administration of high-dose intravenous immunoglobulins (IVIG), e.g., at a dose of 1 g per kg of body weight daily on two consecutive days.
- Diagnostics for HIT/VIPIT should be ordered prior to the administration of IVIG, since high-dose immunoglobulins may lead to false negative test results.

- Regardless of (autoimmune) HIT and VIPIT test results, 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.



Diagnostic and therapeutic algorithm in patients with thrombocytopenia / thrombosis following vaccination with the AstraZeneca COVID-19 vaccine



With friendly recommendation

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