

ISTH Interim Guidance for the Diagnosis and Treatment on Vaccine-Induced Immune Thrombotic Thrombocytopenia (Updated 20 April, 2021)

Step 1: Who is at risk for VITT?

- 1) COVID-19 vaccination 4-28 days prior to onset of symptoms?
 - VITT has only been identified following AstraZeneca or Johnson & Johnson vaccine. It has not been identified after other vaccines.
- 2) Signs/symptoms suggestive of thromboembolism?
Examples include (but not limited to) NEW ONSET:
 - Severe, persistent headache +/- vision change, seizure-like activity
 - Severe, persistent abdominal pain
 - Leg swelling or pain
 - Chest pain and/or shortness of breath

If answers to questions 1 and/or 2 are no, then this is not VITT. Manage clinical presentation according to standard practice.

- If answers to both questions are yes, then proceed to Step 2.

Step 2: How to screen for VITT in at risk patients?

- Order appropriate imaging tests to confirm thromboembolism based on symptom presentation (e.g., CT venogram head for headache, CT venogram abdomen for abdominal pain).
- Order an urgent complete blood count.

If no thrombosis on imaging → this is not VITT.

If platelet count $\geq 150 \times 10^9/L$ → VITT unlikely.

If there is evidence of acute thrombosis AND platelet count $< 150 \times 10^9/L$ → possible VITT proceed to Step 3.

Step 3: Initial evaluation

Order standard coagulation laboratory studies (D-dimer, PT, aPTT and Clauss fibrinogen)

Order immunoassay for platelet factor 4 (PF4) antibodies (not all assays detect this antibody. HIT ELISA is the most reliable).

- If reliable PF4 antibody immunoassay test is negative, VITT is excluded. Treat thrombosis according to standard practice.
- If PF4 antibody immunoassay test is positive, particularly if the optical density reading is high, VITT is likely; arrange confirmatory functional assay for PF4 antibodies (if available) and treat as per VITT (step 4).
- If PF4 antibody immunoassay is not rapidly available, check D-dimer level. Markedly elevated D-dimer levels (e.g., >4x threshold for VTE exclusion) is highly suggestive of VITT. Treat as per VITT (step 4).

Step 4: VITT treatment

- Tests for PF4 antibodies may have a slow turnaround time. DO NOT WAIT for results if diagnosis of VITT seems likely.
- Give intravenous immunoglobulin immediately (0.5 to 1 g/kg daily for 2 days) and consider steroids (e.g., prednisone 1 to 2 mg/kg) if platelet count is less than $50 \times 10^9/L$.
- Avoid platelet transfusions (unless patient requires urgent surgery), heparin, low-molecular-weight heparin, and vitamin K antagonists.
- Give a non-heparin anticoagulant such as fondaparinux, argatroban, or a direct oral anticoagulant (e.g., apixaban, rivaroxaban) if platelet count is over $50 \times 10^9/L$ and there is no serious bleeding.
- Consult an expert in thrombosis, such as hematology or vascular medicine.
- Consider early plasma exchange or fibrinogen substitution to $> 1.0 \text{ g/L}$ if platelet count remains less than $30 \times 10^9/L$ despite intravenous immunoglobulin and steroid treatment or fibrinogen level is less than 1 g/L.

Important notes:

- 1) The management of VITT is evolving. Please ensure you are using an up-to date copy of this living guidance.
- 2) National and/or regional societies and organizations should adapt this guidance to local practice patterns and available resources. It may be useful to generate local lists of laboratories that can perform PF4 antibody immunoassays as well as lists of thrombosis experts who can provide clinical guidance.