

22 November 2021

## **Distinguishing between Thrombosis and Thrombosis with Thrombocytopenia (TTS) following COVID-19 vaccinations**

The topic of thrombosis, specifically in association with thrombocytopenia, has emerged as a concern with the non-replicating adenovirus vector-based vaccines, currently the AstraZeneca and Janssen COVID-19 vaccines. Comirnaty (Pfizer COVID-19 vaccine) is the only COVID-19 vaccine currently in use in New Zealand and is an mRNA vaccine (not an adenovirus vector-based vaccine).

The following information is designed to provide healthcare workers with an understanding of the differences between thrombosis and TTS and does not replace clinical judgement.

***At the current time, Comirnaty has not been found to be associated with a risk of thrombosis with thrombocytopenia syndrome (TTS) in New Zealand or internationally.***

However, there have been reports of thrombosis only following Comirnaty vaccinations. In New Zealand, up to the 28<sup>th</sup> September 2021, the Centre for Adverse Reaction Monitoring (CARM) has received 107 reports of thrombosis (45 deep vein thrombosis, 45 pulmonary embolism, 1 cerebral venous sinus thrombosis, 2 superior mesenteric vein thrombosis, 1 hand thromboembolism, 1 renal thromboembolism, 9 superficial venous thrombosis, and 3 thrombosis of unclear type). There was no evidence of bleeding in any of these cases. Further, a report of thrombosis following vaccination does not necessarily imply a causal link to the vaccine, and often these events occur coincidentally.

Thrombosis occurs commonly in the population. In New Zealand, approximately 800 people per million develop thrombosis each year. The number of cases of thrombosis reported following vaccination with Comirnaty is lower than the expected background rate for thrombosis in New Zealand.

Thrombosis is not currently considered to be an adverse drug reaction associated with Comirnaty. This assessment was endorsed by New Zealand's COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) on 22 July 2021. This was reviewed again by the CV-ISMB on 6 October 2021 and there was no change. Medsafe will continue to monitor this safety signal.

### **What is TTS and how does it differ from thrombosis?**

TTS is a rare newly identified condition. The [Brighton Collaboration](#) draft definition describes the condition as "***any patient presenting with both acute venous or arterial thrombosis AND new onset thrombocytopenia and no known recent exposure to heparin***". The syndrome has some similarity to heparin induced thrombocytopenia (HIT); a rare reaction observed following heparin administration.

See appendix 1 for guidance from the [Thrombosis and Haemostasis society of Australia and New Zealand \(THANZ\)](#) on the identification and treatment of TTS, also referred to as Vaccine induced immune thrombotic thrombocytopenia (VITT).

In TTS, thrombosis often occurs in unusual places such as the cerebral venous sinus and is a serious and potentially life-threatening condition. Notably, patients also have signs or symptoms of mild to severe thrombocytopenia e.g., petechiae. The condition is believed to be immune mediated, with antibodies against platelet factor 4 (anti-PF4 antibodies) detected in most cases. These antibodies are absent in the majority of the general population. Although studies to understand the exact pathology are ongoing, the mechanism is different to that for thrombosis and/or thrombocytopenia.

### **When to suspect TTS?**

- Typically occurs 4 to 42 days post vaccination (adenovirus vector-based vaccines)
- Thrombosis: can be severe and rapidly progressive. Generally, occurring in the cerebral venous sinus or splanchnic veins, although other sites have been reported;  
AND
- Thrombocytopenia ( $<150 \times 10^9$ ): platelets can also be normal on presentation but drop within 4-6 hours <sup>a</sup>
- High D-Dimer (typically very high)
- Reduced fibrinogen
- Positive PF4 ELISA test <sup>b, c</sup>
- No alternative explanation for the condition (i.e., no heparin exposure within the previous 100 days).

### **Note:**

- a. Not all thrombocytopenia post vaccination is TTS, and immune thrombocytopenia has been reported with the COVID-19 vaccines. This is also true for thrombosis, with reports of thrombotic events post vaccination.
- b. PF4 ELISA testing has recently been set up at [LabPlus](#) in Auckland City Hospital. The PF4 ELISA test will be of value for suspected TTS if a patient has received the AstraZeneca or Janssen COVID-19 vaccines within 42 days as per the [THANZ](#) guidance (appendix 1).
- c. In exceptional circumstances, use of the PF4 ELISA test can be discussed with [LabPlus](#) if there is a high level of suspicion of TTS following the Comirnaty vaccine and only after consultation with local haematologists. This is not routine for thrombosis which occurs following Comirnaty vaccine.

### **Risk of TTS**

While no specific risk factors such as age, gender and history of clotting disorders have been detected, most cases of TTS reported globally to date have been female under 60 years of age (median age 41-48 years). Data also suggest that the risk of TTS is much lower after second doses in people who did not experience a problem after the first dose.

### **Clinical case management**

Treatment for TTS is different to standard treatment of thrombosis and should not include heparin. Please refer to the THANZ Advisory Statement: [Suspected Vaccine induced immune](#)

[thrombotic thrombocytopenia \(VITT\)/THANZ Advisory Statement for Haematologists \(check for weekly updates\)](#) for advice on screening and treatment.

## Reporting

All healthcare professionals are encouraged to [report suspected adverse events following immunisation](#) to the Centre for Adverse Reactions Monitoring (CARM)

## Appendix 1.

[Thrombosis and Haemostasis society of Australia and New Zealand \(THANZ\)](#) guidance on identification and treatment of TTS, referred to as Vaccine induced immune thrombotic thrombocytopenia (VITT) below.

**\*Note:** the below link to the VITT/TTS testing form relates to PF4-ELISA testing in Australia. TTS testing (PF4-ELISA test) in New Zealand is performed at [LabPlus](#) in Auckland City Hospital.

