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## Response to correspondence in reference to the previously published Epub manuscript: immune thrombocytopenic purpura after SARS-CoV-2 vaccine

We appreciate the correspondence of Scanvion *et al.* (2021) and their comments on our case report of immune thrombocytopenic purpura (ITP) arisen 22 days after the first dose of vaccination with the ChAdOx1 nCoV-19 vaccine (Oxford–AstraZeneca, Vaxzevria®).<sup>1</sup> They reported two additional cases, both of a woman with a previous history of ITP showing exacerbation of thrombocytopenia after vaccination. However, in both cases, the platelet nadir was never below  $52 \times 10^9/l$ . No haemorrhagic symptom occurred; conversely, our patient had diffuse purpura of the skin and oral mucosa, with a platelet count of  $2 \times 10^9/l$ . After three cycles with dexamethasone 40 mg/day for four days at intervals of 10 days, the platelet count reached a value of  $97 \times 10^9/l$ , and we withdrew steroid treatment. One week later, the platelet count was  $105 \times 10^9/l$ . After publication of the case report, the platelet count dropped to  $55 \times 10^9/l$  (one month after vaccination); a second platelet count the following day was  $63 \times 10^9/l$ . No treatment was started considering the platelet count and the absence of haemorrhagic symptoms. The patient complained of headache and dizziness; the D-dimer value was 4 031 ng/ml. Therefore, a computed tomography (CT) total body scan was carried out, showing no signs of cerebral venous thrombosis or pulmonary embolism, or thrombosis involving abdominal vessels. The assay for anti-PF4 antibodies was negative (HemosIL AcuStar HIT IgG assay, Instrumentation Laboratory, Bedford, MA, USA), and the dilute Russell viper venom time ratio was confirmed positive (DRVVT<sub>r</sub> 1.44). International normalized ratio (INR; 1.06), activated partial thromboplastin time (aPTT; 28.8 s) and fibrinogen (277 mg/dl) were within the normal range. Anticardiolipin and anti-beta2-glycoprotein antibodies were absent.

We should point out the following points:

- 1 *De novo* ITP after vaccination is a well-known condition.<sup>2</sup> A co-incident occurrence of ITP arising after vaccination is possible but unlikely. On Sunday, 14

February 2021, 29 744 individuals had been vaccinated against SARS-CoV-2 in Italy (7 058 with Vaxzevria®; <https://lab24.ilsole24ore.com/numeri-vaccini-italia-mondo/#vaccinazioni-giorno-per-giorno>, accessed 16 May 2021). Considering an annual incidence of 2.9/100 000 person-years<sup>3</sup>, the expected number of cases during three weeks should be one over 602 409, with a likelihood of occurrence of 1.17% in a cohort of 7 058 subjects. Moreover, the patient's platelet count in a blood examination of 2019 was  $208 \times 10^9/l$ . Therefore, we consider a causal relationship with vaccination more likely rather than a co-incidence.

- 2 The recently described VITT (vaccine-induced immune thrombotic thrombocytopenia) syndrome is characterized by the presence of all these four criteria: (i) COVID-19 vaccine (Johnson & Johnson/AstraZeneca *only* to date) 4–30 days previously; (ii) multisite venous or arterial thrombosis (often cerebral or abdominal); (iii) thrombocytopenia; and (iv) positive PF4 'HIT' (heparin-induced thrombocytopenia) ELISA (<https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia>, accessed 16 May 2021). In our patient, the assay for anti-PF4 antibodies was carried out by chemiluminescence, which results negative in many cases positive by ELISA test<sup>4</sup>. However, no thrombosis at atypical sites was detected.

Therefore, we conclude that our patient suffered from vaccine-related isolated immune thrombocytopenia which was partially responsive to steroid treatment. Physicians should be aware that thrombocytopenia after anti-SARS-CoV-2 vaccine may present as an isolated ITP not accompanied by the severe VITT syndrome to avoid undue anxiety. The VITT syndrome is never asymptomatic, but besides petechiae, easy bruising or bleeding it is accompanied also by one or more of the following symptoms related to vessel occlusion: severe headache, visual changes, abdominal pain, nausea and

## Correspondence

vomiting, back pain, shortness of breath, leg pain or swelling.<sup>5-7</sup> The increased D-dimer levels may induce the suspicion of thrombosis, but it may be non-specific and due to an inflammatory response after vaccination. After COVID-19, increased D-dimer levels persist up to four months after the infection<sup>8</sup> so that a similar occurrence can be hypothesized after vaccination. However, in thrombocytopenic cases with D-dimer levels exceedingly high [(above 4 000 FEU fibrinogen equivalent units), i.e., 2 000 ng/ml], investigation for thrombosis is cautiously recommended.<sup>9</sup>

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## Patient consent statement

The patient confirmed his consent for publication of the case.


## Author contributions

MC and ER designed the paper. VDS and FF wrote the first draft of the paper. All the authors revised the manuscript and approved the final form.

## Conflicts of interest

The authors report no conflicts of interest for the submitted manuscript.

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