

Guidance from the UK ITP Forum Working Party on ITP/ITP relapse following Covid-19 vaccination.

Guidance version 2.3 15/06/2022

This is a live document and will be updated as further information comes to light.

Background

In February 2021, 20 cases (1 fatal) of new onset ITP occurring within 1-2 weeks of Covid-19 vaccine (Pfizer, Moderna) were reported in the United States (US) as possible post-vaccine secondary ITP (Lee et al, AJH 2021). Establishing causality can be difficult, especially without case-control data. The authors observed that in the 2 month reporting period, the number of cases were not obviously higher than the anticipated background rate. A Scottish case-control study of 2.53 million people receiving first dose Covid-19 vaccination found a small increased risk of ITP with an estimated incidence of 1.13 cases per 100,000 first doses of AstraZeneca, but no increase after the Pfizer vaccine (Simpson et al, Nat Med 2021). This appeared similar to the risk associated with other vaccines such as Hepatitis B, MMR and influenza.

In patients with existing ITP, the reported risk of relapse following Covid-19 vaccination in three case series was 3-12% (Kuter et al, BJH 2021; Crickx E et al, BJH 2021; Fazzitto B et al 2021). Most relapses were identified between 2 and 7 days.

Reporting outcomes to the Health Security Agency (HSA)

Reporting of new or relapsed ITP cases following Covid-19 vaccination to HSA has now closed. Cases can however be reported as vaccine adverse events to MHRA yellow card scheme at: <https://coronavirus-yellowcard.mhra.gov.uk/>

Guidance on ITP/ITP relapse post following Covid-19 vaccination

Diagnosis

The diagnosis of ITP can be made using standard criteria described in the international consensus guideline (Provan et al Blood Adv 2019).

A diagnosis of post Covid-19 vaccine associated ITP may be considered with presentation or the onset of relevant symptoms within 30 days of vaccination. However, alternative secondary causes should also be considered e.g. infection (including Covid-19), immunodeficiency, and systemic autoimmune or lymphoproliferative disorders.

Another important post-vaccine complication that can occur during this time is Vaccine-induced Immune Thrombocytopenia and Thrombosis (VITT). Updated guidance on VITT is linked from the following webpage: <https://b-s-h.org.uk/about-us/news/guidance-produced-by-the-expert-haematology-panel-ehp-focussed-on-vaccine-induced-thrombosis-and-thrombocytopenia-vitt/>. In cases of suspected post-Covid-19 vaccine ITP, patients should have a clotting screen including Clauss Fibrinogen and D-Dimer. Symptoms or signs of arterial or venous thrombosis should be appropriately investigated.

Treatment

There is currently insufficient published evidence to justify adjustments to previous advice on when to start treatment or the choice of treatment, for ITP (Provan et al Blood Adv 2019) and ITP during the pandemic (Pavord et al BJH 2021). Clinical experience suggests that many cases can either be observed for resolution or respond to typical first line treatments. In contrast, some patients have a more chronic course and require further treatment.

Difficult cases can be discussed with the working group via Teams on Wednesday PM at 14.00.

From 1st February 2022, this meeting will only be on the first week of the month

Link to the meeting:

https://teams.microsoft.com/l/meetup-join/19%3ameeting_MjYyOWQ5OGMtYjE5YS00MTQ2LTk3YjltNzVjNTFIMGZhMTQy%40thread.v2/0?context=%7b%22Tid%22%3a%2237c354b2-85b0-47f5-b222-07b48d774ee3%22%2c%22Oid%22%3a%22ead49e4b-21d0-4ce2-942a-7df928dc069b%22%7d

ITP patients receiving the Covid-19 vaccine

Given the effectiveness of vaccination and the morbidities and mortality from Covid-19 infection, including the risk of Covid-19 associated ITP; ITP is not a contra-indication to vaccination.

ITP has not been identified as a risk factor for VITT and does not influence the decision on vaccine type.

Some patients with ITP will be receiving immunosuppression. Those on immunosuppression are considered an at risk group for COVID-19. Although these individuals may not make a full immunological response to vaccination, it is still recommended

(<https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a>).

In patients with significant thrombocytopenia, a fine needle (23 or 25 gauge) should be used, with sustained pressure at the injection site (without rubbing) for at least 2 minutes to avoid muscle haematoma. Ideally a platelet count of $>20 \times 10^9/L$ is required but a lower platelet count should not preclude it.

In a safety review of Janssen and AZ Covid-19 vaccines, the EMA (European Medicines Agency) recommended platelet count monitoring after vaccination in patients with ITP

(<https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-27-30-september-2021>). As the majority (but not all) patients in the above referenced studies had received Pfizer vaccine, current evidence suggests that ITP relapse is a risk that is not specific to one particular vaccine type. The potential for a fall in platelet count post vaccine should be discussed with patients. A platelet count check should be recommended 2-5 days post-vaccine. Additional FBC checks may be required if the platelet count is falling or bleeding symptoms develop.

With respect to timing of vaccination in patients under consideration for immunosuppression, some useful guidance issued for patients with rheumatological conditions can be accessed here:

<http://arma.uk.net/covid-19-vaccination-and-msk/>

Should patients with ITP or ITP relapse after Covid-19 vaccine receive further vaccinations?

There is limited data on the evolution of ITP after vaccine, and whether a subsequent dose would precipitate a further exacerbation. The data so far suggests that post-vaccine ITP is largely treatment responsive (Lee et al AJH 2021). ITP following first MMR vaccine has not been considered a contra-

indication to second vaccination in US (Miller et al Arch Dis Child 2001) and UK (BSH BJH 2003) guidelines. This remains an active issue with third primary vaccines being offered for immunosuppressed individuals and booster vaccines for others. A review of the evidence submitted to HSA in November 2021 found that a significant minority of patients with ITP/ITP-relapse after COVID-19 vaccine experienced a further significant fall in platelets with rechallenge (27%).

However the benefit of the second vaccine for Covid-19 protection is clear. Furthermore, in the United Kingdom, there has been a rapid rise in the B.1.617.2 (delta) variant. Recent evidence suggests that effectiveness of one Pfizer vaccine was notably lower among persons with the delta variant (30.7%) than among those with the alpha variant (48.7%). The effectiveness of two doses was 88.0% among those with the delta variant compared with 93.7% among persons with the alpha variant. With the AstraZeneca vaccine, the effectiveness of two doses was 67.0% among those with the delta variant and 74.5% among persons with the alpha variant (Lopez-Bernal et al NEJM 2021).

Furthermore, in immunosuppressed patients, reduced vaccine effectiveness against clinical disease was noted after one dose (4%), however, after a second dose of either vaccine, high levels of effectiveness were seen (Pfizer: 73.0%, AstraZeneca 74.6%)

(<https://khub.net/documents/135939561/430986542/RCGP+VE+riskgroups+paper.pdf/a6b54cd9-419d-9b63-e2bf-5dc796f5a91f>).

It is unknown whether switching between Covid-19 vaccines would increase or reduce the risk of ITP recurrence but in the UK, most vaccination will now be with Pfizer and Moderna. Another related area of uncertainty is whether switching vaccines would confer the same clinical effectiveness against Covid-19, as compared to receiving two vaccinations of the same type. Spanish data in pre-print from the CombivacS trial found that of 441 recipients of a first AstraZeneca vaccine who received a second vaccination with Pfizer, 100% exhibited neutralizing antibodies 14 days later, in comparison to 34.1% at enrolment (<https://ssrn.com/abstract=3854768>). In the UK, initial data from the Com-COV study found greater reactogenicity (e.g. fever) with heterogeneous Pfizer & AstraZeneca vaccine schedules (Shaw et al Lancet 2021).

Current evidence therefore suggests that the risk/benefit balance would favour receiving further Covid-19 vaccination in most cases. However the risk/benefit balance should be considered on an individual bases, taking the patients views into consideration and deferral may be considered appropriate in severe and poorly controlled cases of ITP/ITP relapse. If receiving further vaccination, the platelet count should be monitored.

Conclusions:

- **A diagnosis of post Covid-19 vaccine associated ITP may be considered with presentation or the onset of relevant symptoms within 30 days of vaccination.**
- **Consider alternative diagnosis. These include VITT and so check clotting (including Clauss Fibrinogen and D-Dimer), and investigate symptoms or signs of thrombosis.**
- **Treat post Covid-19 vaccine associated ITP along standard lines**
- **ITP patients can receive Covid-19 vaccine, but should be aware of potential relapse risk (3-12%).**
- **If platelets $<50 \times 10^9/L$, a 23 or 25 gauge needle should be used, with sustained pressure for at least 2 minutes.**
- **Platelet count monitoring is now recommended at 2-5 days following Covid-19 vaccination, and if falling platelets or bleeding symptoms develop.**
- **Although risk of further ITP relapse appears higher, patients with ITP/ITP relapse post Covid-19 vaccination may receive subsequent Covid-19 vaccination following: individual risk assessment, patient discussion and with platelet count monitoring**

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