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ORIGINAL ARTICLE

Real-world, single-center experience of SARS-CoV-2 vaccination in immune thrombocytopenia

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Abstract

Background: Immune thrombocytopenic purpura (ITP) relapse following vaccination remains poorly reported in the adult population.

Objectives: This report details real world data from the largest single-center cohort of ITP relapse following severe acute respiratory syndrome (SARS-CoV-2) vaccination.

Methods: The vaccination status of 294 patients under active follow-up was reviewed. A total of 17 patients were identified resulting in an incidence of ITP relapse following SARS-CoV-2 vaccination in this cohort of 6.6% and an incidence of newly diagnosed ITP following SARS-CoV-2 vaccination of 1.4%.

Results: Patients were noted to develop marked deviation of platelet count from baseline following vaccination ($P =< .0001$). Fourteen patients had a prior diagnosis of ITP and median follow-up following diagnosis was 4 years (range 0–45 years). Days from vaccination to presentation ranged from 2–42 (median 14) and the follow-up period was 34 weeks. Fifteen patients (88%) presented with symptoms and all 17 patients developed symptoms during the follow-up period. Nine patients (53%) received a second dose of vaccine during the follow-up period with seven patients (78%) requiring therapeutic support to facilitate second vaccination. Decision to treat patients was multi-factorial and aimed at decreasing bleeding symptoms and obtaining a platelet count $>30 \times 10^9$/L. Sixteen patients (94%) required therapeutic intervention and at the end of the follow-up period, four patients (24%) remained unresponsive to treatment with a platelet count $<30 \times 10^9$/L.

Conclusion: Vaccination of ITP patients continues to have important clinical benefit; however, recommendations for patients who relapse remain lacking. This report outlines the real-world patient outcomes in the era of widespread SARS-CoV-2 vaccination.

KEYWORDS
COVID-19, immune thrombocytopenia, platelets, relapse, vaccination

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1 | INTRODUCTION

Severe acute respiratory syndrome (SARS-CoV-2) was declared a global pandemic in 2019. The disease syndrome (COVID-19) associated with the virus has been linked with significant morbidity and mortality.[1,2] As of June 2021, there have been 3.92 million deaths worldwide and more than 181 million recorded cases.[3] Vaccination remains the current most important factor available to change the course of this pandemic and decrease morbidity and mortality. Vaccines licensed at an unprecedented rate have enabled widespread roll-out of effective protection against the severe effects of SARS-CoV-2.[4–6] Highlighting unexpected outcomes of widespread vaccination within certain patient groups aims to decrease adverse events associated with vaccines within the population[7] and improve patient outcomes.

Immune thrombocytopenic purpura (ITP) is an autoimmune disease characterized by isolated thrombocytopenia (platelet count $<100 \times 10^9$/L)[8] and a hallmark of the condition is no clinical or laboratory features to suggest another underlying or secondary cause.[9,10] Patients with ITP are at higher risk of bleeding events at lower platelet counts and treatment is aimed at decreasing bleeding complications, improving quality of life and decreasing treatment side effects.[11] Thrombocytopenia in COVID-19 infection remains rare (5% in hospitalized patients and 8% in intensive care patients in initial reports of the pandemic)[12] and thrombosis remains an overwhelming hematological feature of the disease course with considerable associated morbidity and mortality.[13]

We report the largest single-center cohort in the United Kingdom of vaccine-induced ITP relapse or new ITP diagnosis following SARS-CoV-2 vaccination. Of note, this new clinical entity within ITP patients following SARS-CoV-2 vaccination differs from the expected hematological challenges that faced ITP patients with COVID-19 disease.[14]

Essentials

1. Relapse of immune thrombocytopenia following severe acute respiratory syndrome (SARS-CoV-2) vaccination is an important cause of relapse in this patient group.
2. The vaccination status of 294 immune thrombocytopenic purpura (ITP) patients under active follow-up was reviewed from January 1, 2021 to August 31, 2021; 211 patients (72%) received SARS-CoV-2 vaccination during this period.
3. The incidence of ITP relapse following SARS-CoV-2 vaccination in this cohort was 6.6% and the incidence of new diagnosis following vaccination was 1.4%; both mRNA and modified adenovirus vaccines were noted to cause relapse.
4. Ninety-four percent of patients required therapeutic intervention at the end of the follow-up period of 34 weeks; 24% of patients remained unresponsive to treatment.

2 | METHODS

Patients with ITP under active follow-up at a single center from January 1, 2021 to August 31, 2021 were reviewed. Inclusion criteria of the final cohort included patients who had undergone recent SARS-CoV-2 vaccination and presented with: significant deviation from baseline platelet count (defined as deviation of >50% from baseline), new marked thrombocytopenia (defined as platelet count $<30 \times 10^9$/L), or new onset of bleeding symptoms. Patients with secondary causes to account for thrombocytopenia were excluded from the cohort and patients who received the ChAdOx1 nCoV-19 (AstraZeneca) vaccine and cases diagnosed with vaccine induced thrombocytopenia and thrombosis (VITT) were excluded. ITP diagnosis was confirmed as per the international consensus guidelines[10] and the American Society of Hematology guidelines.[15] Full blood count analysis was performed on a SYSMEX XN-1000 hematology analyzer (Sysmex Corporation) and all samples were analyzed within 2 h of being taken. Immature platelet fraction (IPF) was analyzed in conjunction with the platelet count for each sample with normal range being between 1% and 5%. Patients attended for blood counts as clinically indicated during the follow-up period.

Treatment responses were analyzed and response to treatment was categorized into three groups as per previously defined categories:[16] complete response (CR)—platelet count rise $>100 \times 10^9$/L; partial response (PR)—platelet count rise $>30 \times 10^9$/L and $<100 \times 10^9$/L; or no response (NR)—platelet count $<30 \times 10^9$/L.

Patients' presenting symptoms were classified (as per previously recognized bleeding score)[17] into three groups (asymptomatic, cutaneous bruising, bleeding [petechiae/mucosal]) and documented during clinical consultations. Mucosal bleeding was further characterized into site (oral mucosal, gastrointestinal, or menorrhagia). Decision to treat was based on established guidelines, specific guidelines,[18] and clinical expertise.

Statistical analysis was performed using GraphPad PRISM version 9 (GraphPad Software). Parametric paired and non-paired *t*-tests were used to compare groups. An alpha value of <0.01 was considered statistically significant.

3 | RESULTS

Of the 294 patients with confirmed primary ITP under active follow-up at a single center in the United Kingdom from January 1, 2021 to August 31, 2021, 211 patients (72%) had received SARS-CoV-2 vaccination during the follow-up period of 34 weeks. Fifteen patients (7%) had declined vaccination and 68 patients (32%) had no vaccination data available. The use of all three licenced vaccines was observed with 53% receiving the BNT162b2 mRNA COVID-19 (Pfizer-BioNTech vaccine; $n = 111$), 27% receiving the ChAdOx1

nCoV-19 (AstraZeneca; $n = 58$), and 1% receiving the mRNA-1273 (Moderna; $n = 2$) vaccine. Of the 211 vaccinated patients 17 patients were noted to have either clinical or laboratory features consistent with ITP relapse or a new diagnosis of ITP following vaccination; 14 of the 17 patients developed relapse of ITP (incidence of 6.6%) and 3 patients presented as newly diagnosed ITP (incidence of 1.4%; Figure 1).

3.1 | Patient characteristics

The 17 patients with laboratory or clinical features of relapse following COVID-19 vaccination, median age for the cohort was 53 years (range; 19–78). Eight patients (47%) were male, and 9 patients (53%) were female. Years since diagnosis of ITP ranged from 0–45 (median 4 years) and age at diagnosis of ITP ranged from 19–70 years (median 38 years). Other comorbidities included previous hypothyroidism not on treatment (2 patients), previous autoimmune hemolytic anemia in remission (1 patient), previous autoimmune neutropenia (2 patients) in remission, hypogammaglobulinemia diagnosed subsequent to the ITP diagnosis (1 patient), previous haematological malignancy in remission, currently in remission (2 patients), and essential hypertension (1 patient). Nine patients had no comorbidities.

Patients with known ITP had undergone multiple treatment regimens (prior to relapse following vaccination) and these included: steroids ($n = 1$), steroids/intravenous immunoglobulin (IVIg; $n = 1$), steroids/IVIg/rituximab ($n = 1$), IVIg/rituximab ($n = 2$), nil therapy ($n = 4$), thrombopoietin receptor agonist (TPO-RA; $n = 3$), steroids/IVIg/TPO-RA ($n = 5$). Current treatment at the time of vaccination included no treatment ($n = 12$), IVIg ($n = 1$), TPO-RA ($n = 4$; 1 patient on romiplostim and 3 patients on eltrombopag; Table 1). No patients who developed relapse post-vaccination had undergone previous splenectomy.

3.2 | Vaccine characteristics

Patients were offered vaccination as per the National Health Service vaccination priority schedule and vaccine availability. Choice of vaccine was determined by availability and age, with patients under 30 years offered the mRNA vaccines as per national guidance, which commenced as of April 2021. Thirteen patients (76%) received the BNT162b2 mRNA COVID-19 (Pfizer-BioNTech), three patients (18%) received the ChAdOx1 nCoV-19 (AstraZeneca), and one patient (6%) received the mRNA-1273 (Moderna). Ten patients (59%) developed an ITP relapse after the first vaccine dose, seven patients (41%) developed an ITP relapse after the second dose of the same vaccine. Three patients were de novo presentations of ITP, two patients presented following vaccination after the first dose of BNT162b2 mRNA COVID-19 (Pfizer-BioNTech), and one patient presented following the second dose of ChAdOx1 nCoV-19 (AstraZeneca) vaccine. Nine patients (53%) received a second COVID-19 vaccine dose during the follow-up period. There was no mixing of vaccines within the cohort. Table 1 summarizes the key features of the cohort.

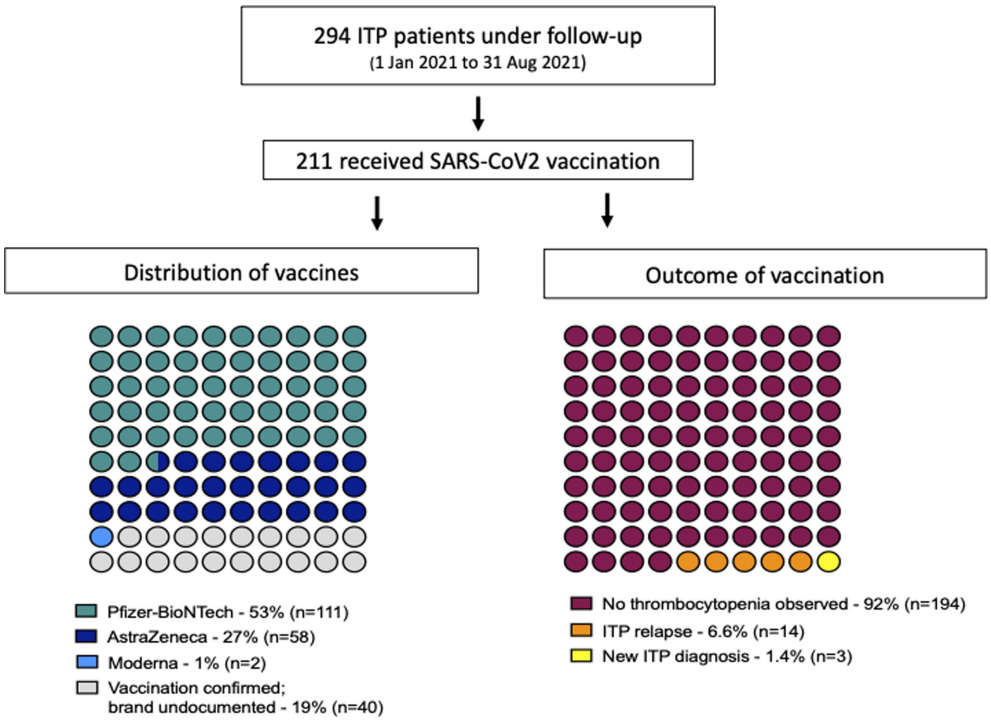

FIGURE 1 Distribution of vaccines and outcomes of the cohort during follow-up period. ITP, immune thrombocytopenic purpura

TABLE 1 Summary of cohort demographics and key management outcomes

Age	19–78 (median 53 years)
Gender	8 males (47%), 9 females (53%)
Age at diagnosis	19–70 years (median 38 years)
Years since ITP diagnosis	0–45 years (median 4 years)
Vaccine dose resulting in presentation	1st dose 10 (59%) 2nd dose 7 (41%)
Vaccines received resulting in relapse/ new diagnosis	• BNT162b2 mRNA COVID-19 (Pfizer-BioNTech)—13 (76%) • ChAdOx1 nCoV-19 (AstraZeneca)—3 (18%) • mRNA-1273 (Moderna)—1 patient (6%)
Incidence of ITP relapse	*n* = 14 (6.6%)
Incidence of new ITP diagnosis	*n* = 3 (1.4%)
Previous ITP treatments	Nil *n* = 4 (24%) Steroids *n* = 1 (6%) Steroids/IVIg *n* = 1 (6%) TPO-RA *n* = 3 (17%) Steroids/IVIg/TPO-RA *n* = 5 (29%) Steroids/IVIg/Anti-CD20 *n* = 1 (6%) IVIg/Anti-CD20 *n* = 2 (12%)
Treatment at the time of vaccination	Nil *n* = 12 (70%) IVIg *n* = 1 (6%) TPO-RA *n* = 4 (24%)
Presenting symptoms	Bruising or bleeding *n* = 15 (88%) Nil *n* = 2 (22%)
Symptoms during follow-up	Mucosal bleeding (*n* = 12), petechiae (*n* = 2), bruising (*n* = 2), and subconjunctival hemorrhage (*n* = 1)
Management	No therapy – *n* = 1 (6%) 1 line of therapy – *n* = 5 (29%) 2 lines of therapy – *n* = 5 (29%) 3 lines of therapy – *n* = 3 (18%) 4 lines of therapy – *n* = 3 (18%).
Outcome at end of follow-up	NR – *n* = 4 (24%) PR – *n* = 3 (17%) CR – *n* = 10 (59%)

Abbreviations: CR, complete response; ITP, immune thrombocytopenic purpura; IVIg, intravenous immunoglobulin; NR, no response; PR, partial response; TPO-RA, thrombopoietin receptor agonist.

3.3 | Laboratory features and symptomology

All patients developed either bleeding symptoms or confirmed new onset thrombocytopenia following vaccination, with no other precipitating cause. Days from vaccine to presentation ranged from 2–42 (median 15). Baseline platelet count for the cohort prior to vaccination count ranged from 30 × 10^9/L – 312 × 10^9/L (median 129 × 10^9/L). Of the 14 patients with historical counts, 9 (53%) were in CR, 5 (47%) were in PR, and no patients had platelet count <30 × 10^9/L. Immature platelet fraction (IPF) was inversely proportional to nadir platelet count ($P = .009$) and ranged from 13.5%–44.5% (median 27.2%). Platelet nadir for the cohort following vaccination ranged from 0 × 10^9/L to 42 × 10^9/(median 6 × 10^9/L) with 16 of the 17 patients (94%) developing a platelet nadir <30 × 10 × 10^9/L. At the end of the follow-up period, the current platelet count for the cohort was a median 104 × 10^9/L (range 4 × 10^9/L–300 × 10^9/L) and 10 patients (59%) achieved a CR. Four patients (24%) remained unresponsive to therapy; however, there was no difference between baseline platelet count and current platelet count ($P = .5$) for the cohort as a whole despite four non-responding patients. Comparing platelet nadir to either baseline platelet count or current platelet count showed a noted difference ($P =< .0001$) highlighting the significance of the platelet nadirs for the cohort following vaccination (Figure 2). Changes in platelet count following vaccine dose 1 and vaccine dose 2 were analyzed. There was no difference between platelet nadir, baseline platelet count, or current platelet count when comparing the two doses (Figure 2).

Fifteen of the seventeen (88%) patients presented with bleeding or bruising symptoms and in two (12%) cases the relapse was subclinical. During the follow-up period, all patients developed symptoms and these included mucosal bleeding (*n* = 12), petechiae (*n* = 2), bruising (*n* = 2), and subconjunctival hemorrhage (*n* = 1). Mucosal bleeding included oral mucosal, lower gastrointestinal bleeding, and menorrhagia.

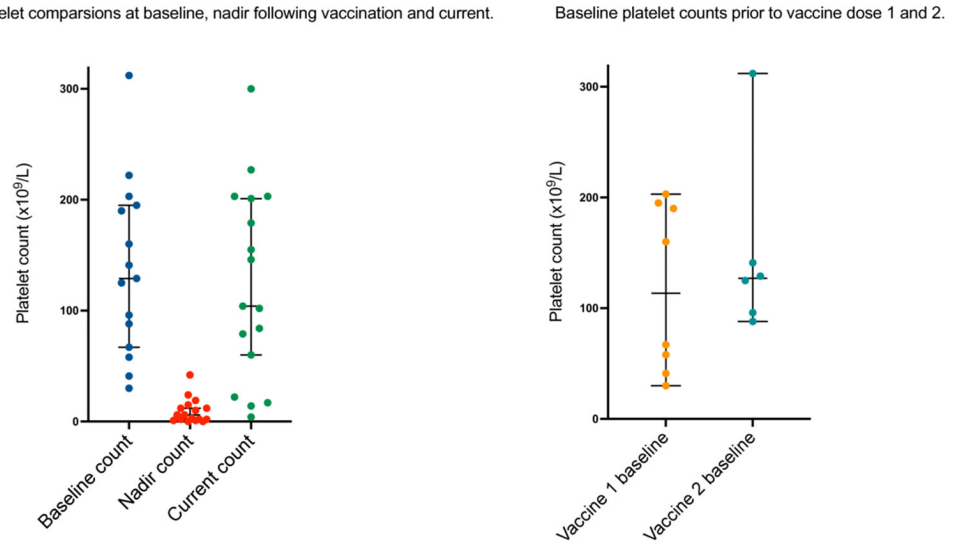

FIGURE 2 Platelet count changes during follow-up period; a marked deviation from baseline was noted for the cohort with generalized recovery to pre-vaccination levels

3.4 | Therapeutic agents and response

The follow-up period for the cohort ranged from 5–24 weeks (median 17 weeks) and ranged from January 1, 2021 to August 31, 2021 (overall combined period of 34 weeks). Treatment regimens following thrombocytopenia after vaccination ranged from 0–4 lines of therapy. Sixteen of the 17 patients (94%) required treatment and 1 patient (who presented with mucosal bleeding) declined therapy and elected close monitoring.

Figure 3 characterizes individual platelet count and highlights relevant treatment events. Five patients (29%) required at least one line of therapy, five patients (29%) required two lines, three patients (18%) required three lines, and three patient (18%) required four lines of therapy. Tranexamic acid (TXA) was used to decrease bleeding symptoms and duration in patients assessed to be high risk. Anti-CD20 therapy was used in three patients and all had documented previous response to rituximab.

Eleven (65%) patients required IVIg and three patients (17%) required more than one dose of 1 gram/kilogram of IVIg. Eight of the eleven (72%) patients who received IVIg achieved either a PR or CR. One patient (12%) received IVIg as monotherapy. Of note the three patients who did not respond to IVIg also remained unresponsive to other attempted lines of therapy. A 100% increase in IVIg use was noted after the initiation of widespread vaccination in ITP patients in our institution compared to the same time period in 2019.

The use of TPO-RA agents (eltrombopag and romiplostim) were important therapeutic agents within this cohort. These allowed for rationing of IVIg and the limiting of steroid use. Ten patients (58%) received TPO-RA therapy and one patient underwent a switch of agents (from eltrombopag to romiplostim) due to lack of response. Of the ten patients who received TPO-RA therapy, six (60%) achieved a CR or PR within the follow-up period.

Nine patients (53%) received both first and second dose of vaccine during the follow-up period. Five (55%) of the nine patients were on regular ITP treatment (four eltrombopag, one romiplostim) at the time of the second vaccine. Following receipt of the second vaccine, three of these patients required rescue IVIg therapy due to the development of a platelet count $<30 \times 10^9$/L.

Seven patients received only the second dose of vaccine during the follow-up period and all seven required therapeutic support following second vaccination. Six of the seven patients (85%) developed a platelet nadir $<30 \times 10^9$/L and one patient was treated at a platelet nadir of 40×10^9/L due to bleeding symptoms.

Time to treatment response was variable between patients. After 34 weeks (at the end of the follow-up period), four (24%) of patients continued to have NR to therapy, three patients (17%) had a PR to treatment, and ten patients (59%) had a CR to treatment.

Four patients remained unresponsive to treatment (Figure 3; patients 3, 10, 11, 14). Of the four non-responsive patients, two patients had a platelet count $<100 \times 10^9$/L prior to vaccination (88×10^9/L and 96×10^9/L) and two patients had a platelet count $>100 \times 10^9$/L prior to treatment (190×10^9/L and 312×10^9/L). Three out of the four patients in the non-responding group experienced bleeding symptoms at presentation. At the time of end of follow-up one patient continued to experience bleeding symptoms and one patient experienced bruising symptoms.

4 | DISCUSSION

The current COVID-19 pandemic, caused by a novel coronavirus (SARS-CoV-2), posed difficulties in the management of patients with ITP. Guidance early on in the pandemic was released by the British Society of Haematology.[18] This supported clinicians in the management of newly diagnosed ITP during the pandemic and

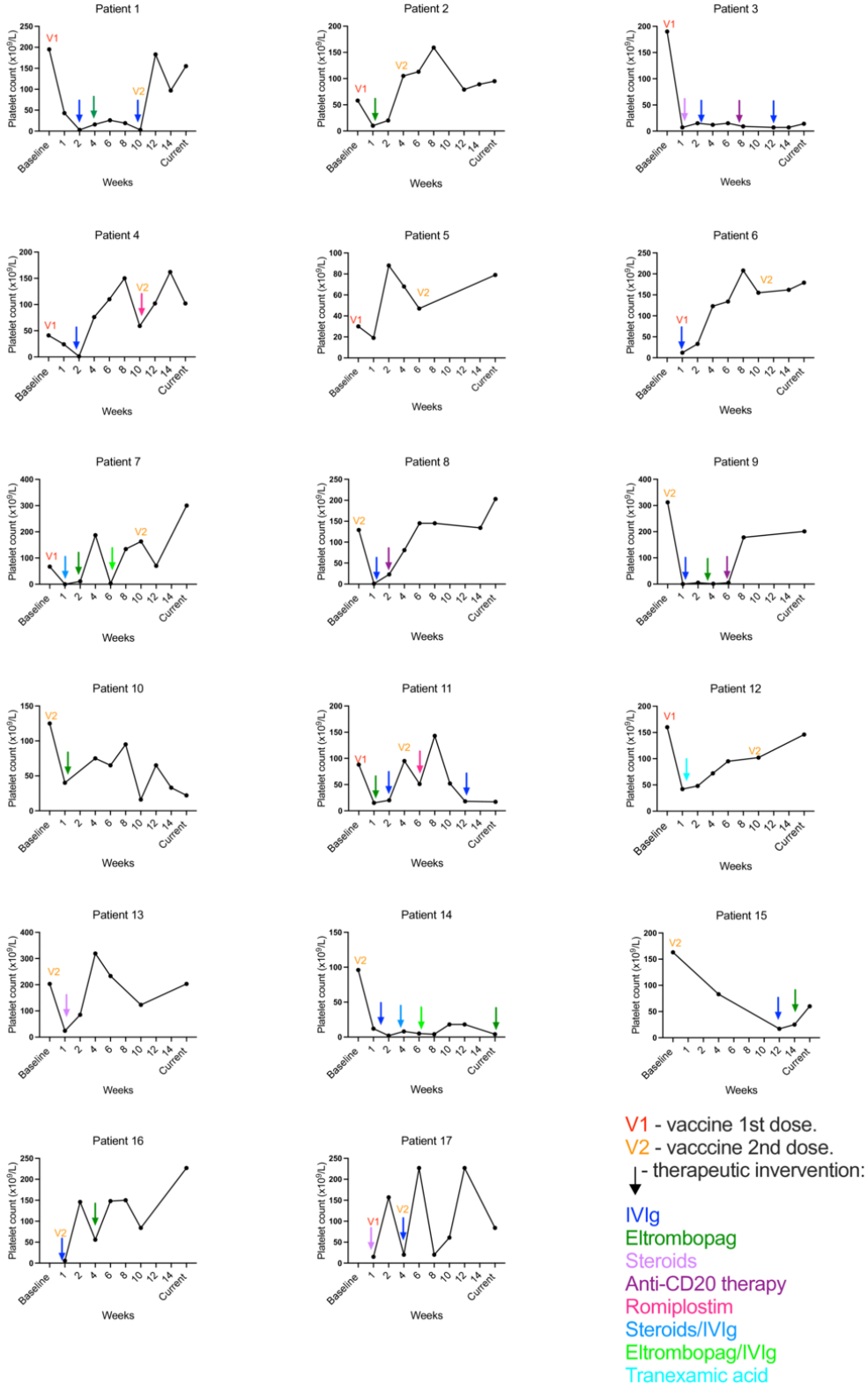

FIGURE 3 Individual platelet trends for cohort during the follow-up period. Vaccine dose 1 (V1) and vaccine dose 2 (V2) are shown and each arrow denotes a therapeutic intervention. Eight combinations of treatment are shown with subsequent platelet response

advocated early use of TPO-RA agents in SARS-CoV-2–negative patients, the addition of IVIg in the initial period if clinically indicated, use of TXA and rapid steroid wean if steroids were used. ITP patients have a heterogenous range of symptoms, relapse rates, and previous treatment agents (including immunosuppression). ITP relapse or new diagnosis following vaccination is an emerging trend in clinical practice[19] and the aim was to report real-world outcomes in ITP patients after the introduction of

widespread SARS-CoV-2 vaccination. To ensure relapse due to vaccination was not overestimated, diagnosis of relapse was carefully distinguished using clear parameters (which have been observed in other cohorts).[20–22] Based on the current evidence, high suspicion of relapse should be considered when any of the following occur within 30 days of vaccination: new bleeding symptoms, platelet count $<30 \times 10^9$/L, and a drop in platelet count >50% from baseline.

The development of ITP has been noted after vaccines to several infectious agents[23] and most data come from pediatric cohorts;[24] 80% of affected children will have a self-limiting clinical course with recovery within 2 months.[25] An incidence of ITP relapse of 6.6% and new ITP diagnosis of 1.4% was noted in this cohort following vaccination. Valuable and recent reviews in this area suggest the risk of relapse appears to vary in the region between 3.3% and 12% and this is important information when counselling and ensuring follow-up of patients.[21,26,27] We note numerous similarities in this cohort to recent reports; of note a large proportion of patients appear to require treatment (93% in one cohort) and encouragingly response rates to treatments are high.[20] This cohort did not consist of patients who had undergone splenectomy; however, there is evidence this group has higher risk of relapse and warrants close monitoring post-vaccination.[20] Time to presentation appears to vary[20,21,26] and a diagnosis of vaccine-induced ITP or relapse following vaccination should be considered in any patient who received a vaccine in the last 30 days.

Of the three most widely available vaccines in the United Kingdom, thrombocytopenia was noted in all three vaccines. Most patients (76%) received the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine within our cohort. The over-representation of this vaccine in the cohort is likely multifactorial. Two important considerations are that this was the first SARS-CoV-2 vaccine available in the United Kingdom and use of the ChAdOx1 nCoV-19 (AstraZeneca) vaccine has been excluded in patients <40 years of age. A population-based analysis observed increased risk of developing thrombocytopenia after ChAdOx1 nCoV-19 (AstraZeneca) vaccine and this was not seen with the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine;[28] however, subsequent reports (including observation from this cohort) confirm relapse in all licensed vaccines have been noted.[21,22,26] Reporting of new safety signals through robust systems remains an important aspect of patient safety in mass vaccine roll-out. The United Kingdom's Medicines and Healthcare Products Regulatory Agency encourages the ongoing and open reporting of events; however, it should be noted that this system cannot derive side effect rates or compare safety profiles between vaccines as many factors influence this kind of reporting system.

Management of patients with relapsed ITP can be a difficult clinical scenario and an individual approach is often recommended given the heterogeneity of the disease and varying response to different treatment agents available. This clinical scenario becomes even more complex when these relapses are associated with a required vaccine within the context of a global pandemic. Seventy percent of patients in this cohort were not on treatment at time of relapse and we found no correlation between baseline platelet count or dose of vaccine received (first or second) and response to treatment. This suggests that monitoring of patients after SARS-CoV-2 vaccination would be appropriate given the lack of predictive tools. Each patient within the cohort had an individualized management plan discussed in a multi-disciplinary team setting to ensure the most appropriate agent combination was chosen. Discussion centered around decreasing treatment side effects as much as possible. Decision to treat patients was based on presenting symptoms, platelet count, previous responses to treatment, patient choice/lifestyle, and comorbidities. Agent choice was primarily based on previous response to therapy in historic (non–vaccine-related) relapses. Aim of therapy included alleviation of symptoms and obtaining a platelet count $>30 \times 10^9$/L. The number of therapeutic combinations (and varying response within the cohort) highlights the clinical challenges faced when treating SARS-CoV-2 vaccine-associated ITP relapse.

The three de novo cases were treated as per standard ITP treatment protocols with exclusion of alternate diagnosis (including VITT). All three patients achieved a complete or partial response to treatment (with two patients requiring TPO-RA therapy) suggesting (in this cohort) there does not appear to be a treatment-resistant nature to vaccine-induced ITP and current therapeutic approaches are appropriate. Interestingly, the four patients who continued to remain unresponsive to treatment at the end of the follow-up period all had stable ITP in remission prior to vaccination; two patients were on TPO-RA therapy at the time of relapse and two were not on treatment. The choice of treatment regimens was drawn from current established guidelines; however, this group posed a difficult clinical scenario, as within the cohort these patients continued to experience adverse effects of vaccination. These patients require ongoing platelet monitoring and psychological support, especially given these lasting side effects remain unexpected and response to available therapy remains unpredictable.

Initial response to IVIg was as expected, with 72% receiving a PR or CR and use was in patients as first-line therapy for acute relapse or symptoms and to enable receipt of second vaccine. As with relapses noted out of the vaccine setting, patients required other agents to sustain a response and this was individually assessed on a patient-by-patient basis with previous response history and other comorbidities taken into account. TPO-RA's were an important therapeutic agent with response rates of 60% allowing for shorter steroid courses and decreased use of immunosuppressive agent.

All patients were strongly encouraged to complete the vaccine course with the same vaccine. Nine patients received both the first and second vaccine dose during the follow-up period and in this group three patients required rescue IVIg therapy due to relapse (platelet nadir $<30 \times 10^9$/L). One patient achieved a sustained CR, one patient achieved a PR, and one patient continued to be non-responsive at the end of the follow-up period. All seven patients who received the second dose during the follow-up period required treatment. Due to this, it is noticed within the cohort that a less pronounced drop in platelet count after second vaccine dose could be attributed to pre-emptive management in patients.

It is acknowledged that there are limitations to this real-world review. First, it is a reflection of a single-center observation and it is widely accepted that multi-center experience gives a better representation of patterns within patient groups. Given the heterogeneity and individual nature of treatment plans for patients with ITP, many treatment options within a small group are often observed making direct comparison to effects of treatment difficult. This was observed in this cohort with patients having undergone multiple and various treatment regimens prior to relapse following SARS-CoV-2 vaccination. As with any evolving practice in the absence of guidelines, it is acknowledged that not all patients underwent identical follow-up procedures thereby making direct comparisons at certain time points difficult. Despite these limitations, there is merit and importance in reporting the real-world experience in evolving clinical situations such as this one described.

Clinical recommendations for the management of vaccine-associated ITP relapse are required for these patients. Based on the experience with this cohort we would recommend the following when considering the management of ITP relapse in the context of SARS-CoV-2 vaccination. Given the high rate of symptoms in the cohort (all 17 patients), ITP patients should have access to close monitoring following SARS-CoV-2 vaccination at standardized time points. Clinicians should have a low threshold for interim full blood count testing should a patient develop symptoms of relapse. Patients should have a comprehensive treatment history taken with initiation of the same agents that were known to illicit a previous documented platelet response (either complete or partial). Clinicians should encourage patients to complete the vaccination course with the same vaccine and therapeutic and psychological support should be offered if required. The use of rituximab in the COVID-19 era was carefully considered. Use was limited only to patients who had trialed other lines of therapy and who had a documented previous response to anti-CD20 therapy. Clinicians understood that poor immune response to vaccination would be expected[19] if given within 2 weeks of the vaccine dose and this was avoided. Many ITP patients remain dependent on immunosuppressive therapy as therapeutic options and vaccination remains important to this group in preventing severe COVID-19 disease. Patients on immunosuppressive therapy should be made aware a complete immunological response to vaccination may not be elicited and the role of antibody monitoring in this group is available; however, the role of this is currently unclear.

It is likely vaccine extension to younger age groups and booster doses are going to become another aspect in the prevention of further surges in COVID-19 in the future. ITP patients with known vaccine-associated relapse will require additional clinical support including monitoring following further vaccination against COVID-19 and reporting such events to relevant regulatory bodies remains essential.

5 | CONCLUSION

SARS-CoV-2 vaccine-associated ITP relapse is not common, but requires patients to be informed and monitored. In our experience, the incidence of ITP relapse was 6.6% and new diagnosis following vaccination was 1.4%. Ninety-four percent of patients who relapse following vaccination required therapeutic intervention. All patients experienced symptoms of bleeding or bruising and a proportion of patients in this cohort (24%) did not recover their platelet counts to pre-vaccination levels after a median of 17 weeks. The benefit of vaccination continues to outweigh any observed adverse outcomes; however, a small group of ITP patients will require intervention following vaccination and should be counseled appropriately.

CONFLICT OF INTEREST

P. Woolley, A. Tailor, and R. Shah report no conflicts of interest. J-P. Westwood: Novartis (Honoraria). M.A. Scully: Ablynx (consultancy, honoraria, other: member of advisory board, research funding, and speaker's bureau), Alexion (honoraria, member of advisory board, and speaker's bureau), Shire (honoraria, member of advisory board, research funding, and speaker's bureau), Novartis (honoraria, member of advisory board, and speaker's bureau), Baxalta (research funding).

AUTHOR CONTRIBUTIONS

P.W. designed the research, collected data, analyzed and interpreted data, performed statistical analysis, wrote the manuscript. A.T. collected data, analyzed data. R.S. collected data, analyzed data. J.-P.W. designed the research, analyzed and interpreted data. M.S. designed the research, analyzed and interpreted data, wrote the manuscript.

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