SUPPLEMENTARY MATERIAL
De novo and relapsed immune thrombocytopenia after COVID-19 vaccines: results of French safety monitoring

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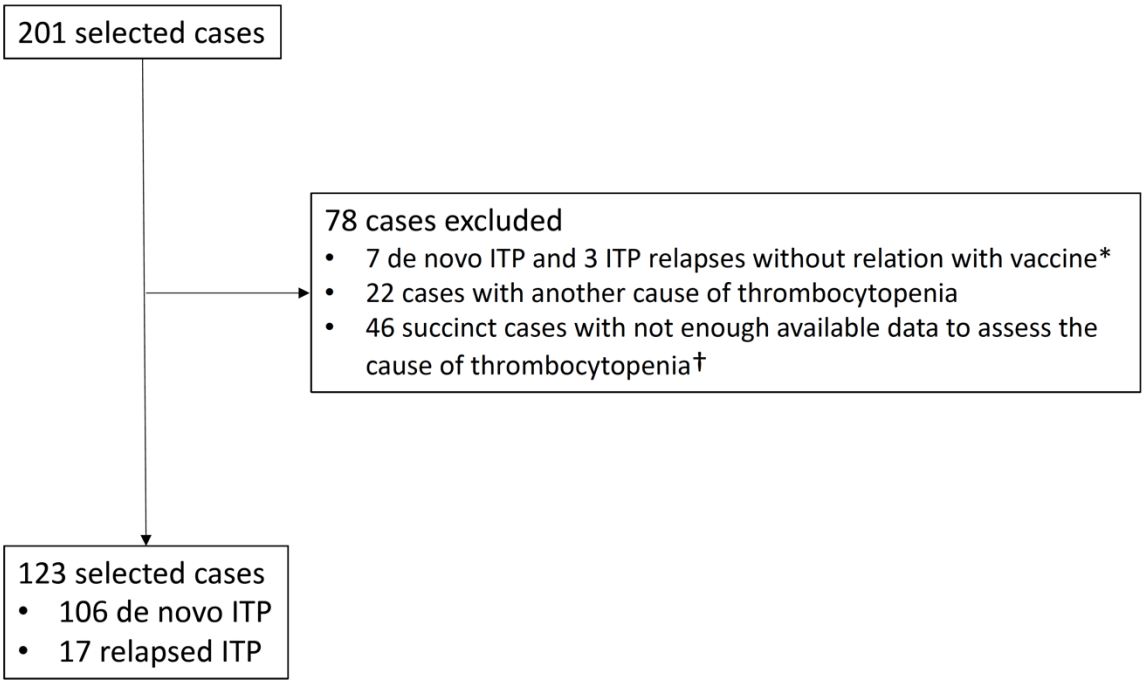

Figure S1. Flowchart of case selection after review by two ITP experts.
*Mostly due to a longer time from vaccine to the event.
†Usually mild thrombocytopenia without further investigation.

Table S1. Description of the two cases of intracranial hemorrhages that occurred.

Case	Description
#1	A 84-year-old woman with Alzheimer disease and a history of ischemic stroke developed ITP 20 days after a first dose of BNT162b2 with a platelet count of 1 x 10^9/L, petechiae, bruises, asymptomatic frontal 5 mm bleed on cranial computed tomography, with favorable response to corticosteroids and IVIg (categorized as certain de novo ITP).
#2	A 63-year-old man with chronic lymphocytic leukemia and severe arterial hypertension was admitted for intracranial bleed ten days after a second dose of BNT162b2; platelet count was normal at admission but dropped four days later to 9 x 10^9/L, responsible for major aggravation of the intracranial bleed and eventually death (categorized as probable de novo ITP).

Table S2. Characteristics of cases of de novo immune thrombocytopenia (ITP) following COVID-19 vaccination by groups of certain and probable ITP.

Characteristics	**Certain ITP (n=58)**	**Probable ITP (n=48)**
Median age, years (min-max)	67 (16-94)	69 (17-98)
Women, n (%)	33 (56.9)	24 (50.0)
History of autoimmune disease, n (%)*	11 (18.9)	12 (16.7)
Vaccine		
BNT162b2, n (%)	35	23
ChadOx1-S, n (%)	20	25
mRNA-1273, n (%)	2	0
Ad26COV2, n (%)	1	0
Dose†		
1, n (%)	41 (73.2)	33 (70.2)
2, n (%)	15 (26.8)	14 (29.8)
Median time to ITP onset, days (min-max)	12 (1-40)	10 (2-40)
Median lowest platelet count, x 10^9/L (min-max)‡	4 (0-36)	15 (1-87)
Bleeding§		
No bleeding, n (%)	3 (5.4)	16 (34.8)
All bleeding, n (%)	53 (94.6)	30 (65.2)
Mouth bullae, n (%)	20 (35.7)	2 (4.4)
Epistaxis, n (%)	6 (10.7)	0
Hemoptysis, n (%)	1 (1.8)	0
Intracranial, n (%)	1 (1.8)	1 (2.2)
Evolution and treatment¶		
Spontaneous recovery, n (%)	1 (1.9)	10 (30.3)
Recovery after corticosteroids ± IVIg only, n (%)	40 (76.9)	16 (48.5)
Recovery after need of TPORAs as second-line treatment, n (%)	8 (15.4)	1 (3.0)
Recovery after need of rituximab as second-line treatment, n (%)	1 (1.9)	2 (6.1)
Recovery after need of dapsone as second-line treatment, n (%)	1 (1.9)	0
Recovery after TPORA first, n (%)	0	1 3.0)
Active disease after corticosteroids without further follow-up, n (%)	2 (3.8)	3 (9.1)
Exposure to another dose of vaccine		
Relapse of ITP, n	2	1
No relapse of ITP, n	1	3
Absence of subsequent exposure to the vaccine, n	36	18
Unknown, n	19	26

Abbreviations: IVIg, intravenous immunolglobulin; ITP, immune thrombocytopenia; TPORA, thrombopoietin receptor agonist.

* 5 patients with thyroiditis (including 2 Graves' disease), 2 with thyroiditis + psoriasis, 1 with thyroiditis + rheumatoid arthritis, 1 with systemic lupus erythematosus, 1 with sarcoidosis, 1 with granulomatosis with polyangitis, 1 with autoimmune hemolytic anemia, 1 with rheumatoid arthritis, 1 with polymyalgia rheumatica, 1 with primary biliary cirrhosis + Biermer anemia, 1 with Behçet disease, 1 with multiple sclerosis 1 type 1 diabetes mellitus and 1 with extramembanous glomerulonephritis.
† 3 missing values (certain ITP, n=2; probable ITP, n=2).
‡ 1 missing value (certain ITP).
§ 4 missing values (certain ITP, n=2; probable ITP, n=2).
¶ 21 missing values (certain ITP, n=6; probable ITP, n=15).

Table S3. Incidence de novo/relapsed immune thrombocytopenia (ITP) within the six weeks after COVID-19 vaccination reported by number of vaccine doses dispensed.

Characteristics	Number of reported cases	Number of doses dispensed	Number of reported cases by 1,000,000 doses (95% CI)
All doses			
All de novo/relapsed ITP	123*	72,752,106	1.69 (1.42-2.01)
BNT162b2 (Pfizer-BioNTech)	70†	57,232,186	1.22 (0.97-1.54)
ChadOx1-S (AstraZeneca)	47‡	7,679,746	6.12 (4.63-8.04)
mRNA-1273 (Moderna)	5§	6,996,846	0.71 (0.30-15.60)
Ad26COV2 (Janssen)	1¶	843,328	1.19 (0.02-0.67)
After Dose 1			
All de novo/relapsed ITP	86	41,673,001	2.06 (1.67-2.55)
BNT162b2 (Pfizer-BioNTech)	41	32,450,088	1.26 (0.93-1.71)
ChadOx1-S (AstraZeneca)	41	4,358,285	9.41 (7.00-12.50)
mRNA-1273 (Moderna)	4	4,021,300	1.00 (0.39-2.54)
Ad26COV2 (Janssen)	-	843,328	-
After Dose 2			
All de novo/relapsed ITP	34	30,998,538	1.10 (0.79-1.53)
BNT162b2 (Pfizer-BioNTech)	28	24,710,406	1.13 (0.78-1.63)
ChadOx1-S (AstraZeneca)	5	3,319,256	1.51 (0.06-3.48)
mRNA-1273 (Moderna)	1	2,968,876	0.34 (0.06-1.89)
Ad26COV2 (Janssen)	0	0	-
After Dose 3			
All de novo/relapsed ITP	0	80,567	-
BNT162b2 (Pfizer-BioNTech)	0	71,692	-
ChadOx1-S (AstraZeneca)	0	2,205	-
mRNA-1273 (Moderna)	0	6,670	-
Ad26COV2 (Janssen)	0	0	-

*106 de novo (74 after Dose 1 and 29 after Dose 2; 3 missing values) and 17 relapsed ITP (12 after Dose 1 and 5 after Dose 2). No case of ITP was reported after Dose 3 during the study period.
†58 de novo (34 after Dose 1 and 23 after Dose 2; 1 missing value) and 12 relapsed ITP (7 after Dose 1 and 5 after Dose 2).
‡45 de novo (39 after Dose 1 and 5 after Dose 2; 1 missing value) and 2 relapsed ITP (after Dose 1).
§2 de novo (1 after Dose 1 and 1 after Dose 2) and 3 relapsed ITP (after Dose 1).
¶1 de novo (Dose rank unknown) and no relapsed ITP.