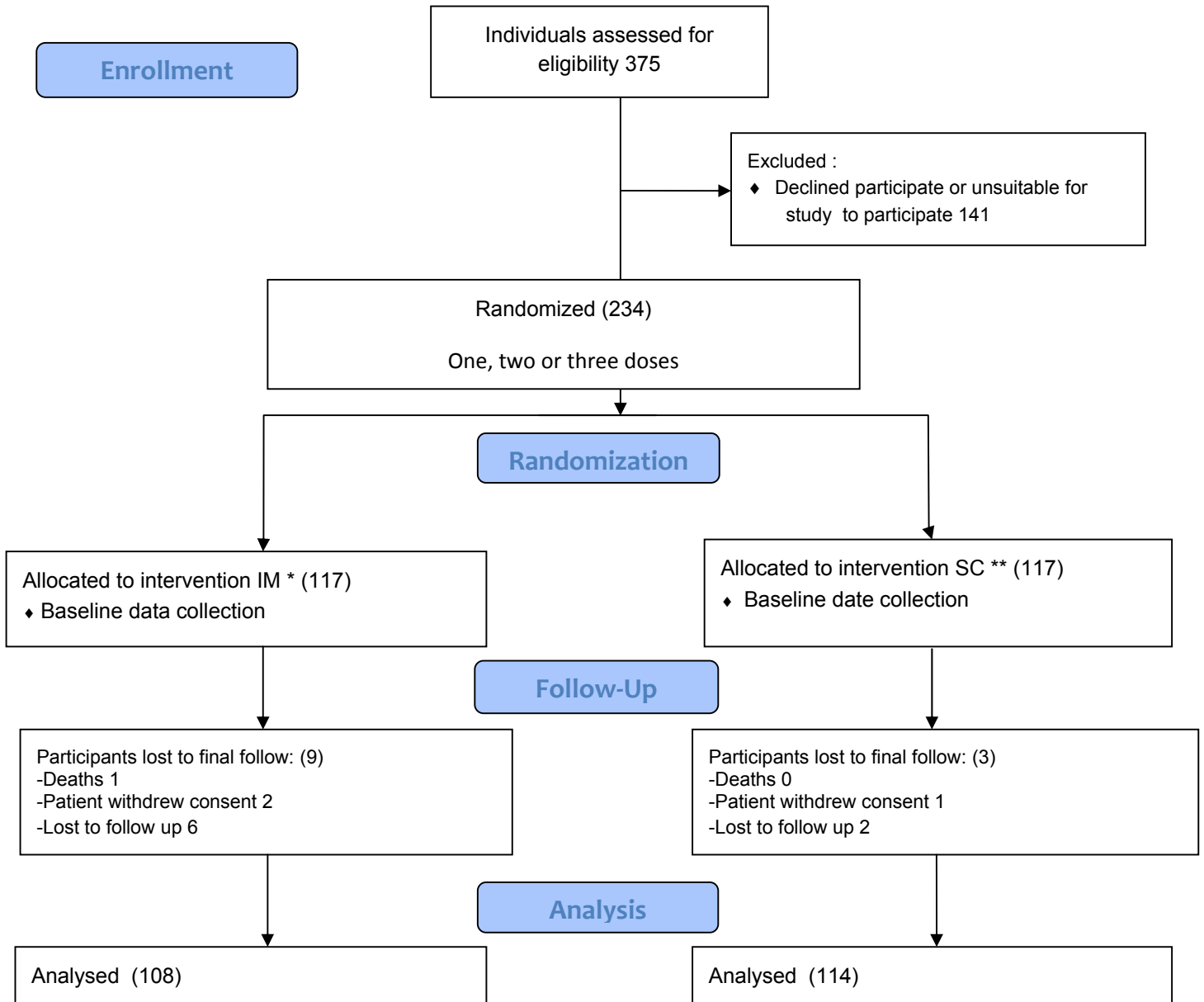


Participant Flow



* IM: intramuscular injection
** SC: subcutaneous injections

Baseline characteristics

	Intramuscular group (n = 108)	Subcutaneous group (n – 114)	Total (n = 222)
Age (years) mean (SD)	71.63 ± 11.39	72.51 ± 9.02	72.07 ± 10.26
Gender : males	67 (57.2%)	65 (55.5%)	132 (56.4%)
Gender: females	50 (42.8%)	52 (44.5%)	102 (42.8%)
Race - Caucasian	100%	100%	100%
Distribution according to vaccine dose number	A dose 84 Two doses 8 Three doses 16	A dose 93 Two doses 5 Three doses 16	A dose 177 Two doses 13 Three doses 32
Basal INR (SD)	2.39 (0.59)	2.5 (0.52)	2.44 (0.56)
Basal antitoxoid tetanus antibodies mUI/ml (SD)	800.2 (1092,9)	922.5 (1148.2)	862.17 (1120.47)
Basal brachial perimeter mm (SD)	367.29 (59.07)	367.31 (66.02)	367.3 (62.53)
Patients without immunity (basal antitoxoid tetanus antibodies < 10 mUml)	22	19	41

Outcome measures

First dose of vaccine		Intramuscular group (n = 108)	Subcutaneous group (n – 114)	P value
Increase in antitetanus antibodies following vaccination mUI/ ml Mean (SD)		2655.56 (1625,8)	2603,63 (1659,1)	0.247 *
Increase in antitetanus antibodies following vaccination (number of times the concentrations are increased) Mean (SD)		87.36 (183.7)	72.09 (178.7)	0.906 *
Patients without immunity Increase in antitetanus antibodies following vaccination mUI/ ml Mean (SD)		2875 (1819.4)	2661.3 (2000.7)	0.683 *
Patients without immunity Increase in antitetanus antibodies following vaccination (number of times the concentrations are increased) Mean (SD)		327.3 (202.5)	281.2 (225.5)	0.584 *
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 1 day follow up	Pain	42	29	0.039 **
	Redness	5	22	0.001 **
	Swelling	9	22	0.014 **
	Heat	10	18	0.117 **
	Granulomas	7	8	0.790 **
	Haematoma	2	4	0.421 **
Appearance of basic injuries in the area of administration of the vaccine (intensity) 1 day follow up	Pain intensity (scale 1 to 10)	0.9 (1.49)	0.72 (1.48)	0.097 *
	Redness size mm (SD)	1.86 (11.4)	5.2 (19.5)	0.001 *
	Size of swelling mm (SD)	1.26 (6.01)	2.93 (9.3)	0.019 *
	Size of haematoma mm (SD)	0.45 (3.3)	0.22 (2.2)	0.677 *

	Size of granuloma mm (SD)	0.9 (0.9)	2.74 (1.16)	0.184 *
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 2 day follow up	Pain	34	28	0.306 **
	Redness	10	22	0.024 **
	Swelling	11	25	0.012 **
	Heat	12	17	0.345 **
	Granulomas	7	8	0.790 **
	Haematoma	1	2	0.562 ***
Appearance of basic injuries in the area of administration of the vaccine (intensity) 2 days follow up	Pain intensity (scale 1 to 10)	0.8 (1.56)	0.60 (1.37)	0.289 *
	Redness size mm (SD)	2.9 (13.03)	6.8 (22.23)	0.016 *
	Size of swelling mm (SD)	2.39 (10.41)	7.62 (38.7)	0.18 *
	Size of haematoma mm (SD)	0.25 (2.57)	0.072 (0.67)	0.574 *
	Size of granuloma mm (SD)	0.09 (0.95)	0.36 (2.29)	0.182 *
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 14 day follow up	Pain	4	5	0.576 ***
	Redness	1	0	0.5 ***
	Swelling	1	3	0.311 ***
	Heat	1	0	0.5 ***
	Granulomas	0	1	0.536 ***
	Haematoma	1	0	0.5 ***
Appearance of basic injuries in the area of administration of the vaccine (intensity)	Pain intensity (scale 1 to 10)	0.2 (0.5)	0.07 (0.26)	0.034 *
	Redness size mm (SD)	0.051 (0.55)	0	0.317 *

14 days follow up	Size of swelling mm (SD)	0.18 (0.19)	0.23 (1.41)	0.314 *
	Size of haematoma mm (SD)	0.18 (1.89)	0	0.317 *
	Size of granuloma mm (SD)	0.018 (0.19)	0.11 (0.89)	0.555 *
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 30 day follow up	Pain	1	2	0.55 ***
	Redness	0	0	N/A
	Swelling	0	0	N/A
	Heat	0	0	N/A
	Granulomas	0	1	0.5 ***
	Haematoma	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 30 days follow up	Pain intensity (scale 1 to 10)	0.04 (0.19)	0.04 (0.21)	0.776 *
	Redness size mm (SD)	0	0	N/A
	Size of swelling mm (SD)	0	0	N/A
	Size of haematoma mm (SD)	0	0	N/A
	Size of granuloma mm (SD)	0	0.071 (0.75)	0.326 *
Axillary node		It was not described in any patient		
Increase of the brachial perimeter mm Mean (SD) 1 day follow up		2.59 (6.13)	4.76 (14.45)	0.769 *
Increase of the brachial perimeter mm Mean (SD) 2 days follow up *		2.45 (7.1)	4.51 (13.6)	0.915 *
Increase of the brachial perimeter mm Mean (SD) 14 days follow up		3.03 (13.02)	1.99 (13.66)	0.708 *
Increase of the brachial perimeter mm Mean (SD) 30 days follow up		0.38 (32.9)	2.37 (14.9)	0.973 *

Emergence of general symptom (number of cases) 1 day follow up	Fever	3	2	0.492 ***
	Malaise	8	2	0.048 ***
	Headache	4	1	0.179 ***
	Weakness	3	1	0.304 ***
	Arthralgias	1	0	0.496 ***
Emergence of general symptom (number of cases) 2 days follow up	Fever	3	4	0.510 ***
	Malaise	6	1	0.057 ***
	Headache	2	1	0.493 ***
	Weakness	4	0	0.059***
	Arthralgias	2	0	0.244 ***
Emergence of general symptom (number of cases) 14 days follow up	Fever	0	1	0.5 ***
	Malaise	0	0	N/A
	Headache	1	2	0.5 ***
	Weakness	1	0	0.5 ***
	Arthralgias	0	1	0.5 ***
Emergence of general symptom (number of cases) 30 days follow up	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	1	0	0.491 ***
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
Any serious adverse effect (one that was fatal or posed danger to patient'		0	0	N/A

life, ended in disabilities or required hospitalization.)			
INR modification after vaccination Mean (SD)	0.12 (0.63)	0.79 (0.72)	0.637 ****
INR modification after vaccination Number of cases with increase Number of cases with decrease Number of cases without change	58 42 9	58 40 9	0.985 **
* Mann–Whitney U test (does not fit the normal distribution) ** Chi-squared test *** Fisher's exact test **** Student's-t test (normal distribution) N/A not applicable			

Second dose of vaccine		Intramuscular group (n = 29)	Subcutaneous group (n = 23)	P value
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 1 day follow up Second dose	Pain	2	4	0.248 ***
	Redness	1	4	0.117 ***
	Swelling	0	3	0.085 ***
	Heat	0	2	0.221 ***
	Granulomas	1	0	0.732 ***
	Haematoma	1	1	0.524 ***
	Axillary node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 1 day follow up Second dose	Pain intensity (scale 1 to 10)	0.68 (1.17)	0.7 (1.26)	0.862 *
	Redness size mm (SD)	0.227 (0.87)	4.3 (12.04)	0.273 *
	Size of swelling mm (SD)	0.227 (1.06)	3.3 (10.29)	0.117 *
	Size of haematoma mm (SD)	0.045 (0.21)	0.5 (0.22)	0.946 *
	Size of granuloma mm	0.045 (0.21)	0	0.340 *

	(SD)			
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 2 days follow up Second dose	Pain	2	3	0.422 ***
	Redness	1	4	0.117 ***
	Swelling	0	3	0.085 ***
	Heat	0	2	0.221 ***
	Granulomas	0	0	N/A
	Haematoma	0	1	0.476 ***
	Axillary node	0	1	0.476 ***
Appearance of basic injuries in the area of administration of the vaccine (intensity) 2 days follow up Second dose	Pain intensity (scale 1 to 10)	0.41 (0.8)	0.25 (0.2)	0.743 *
	Redness size mm (SD)	0.045 (0.21)	4.8 (12.9)	0.12 *
	Size of swelling mm (SD)	0.045 (0.21)	4.3 (11.59)	0.052 *
	Size of haematoma mm (SD)	0	0.050 (0.22)	0.294 *
	Size of granuloma mm (SD)	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 14 days follow up Second dose	Pain	3	3	0.620 ***
	Redness	0	0	N/A
	Swelling	0	0	N/A
	Heat	0	0	N/A
	Granulomas	0	0	N/A
	Haematoma	0	0	N/A
	Axillary node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity)	Pain intensity (scale 1 to 10)	0.23 (0.43)	0.15 (0.37)	0.529 *
	Redness size	0	0	N/A

14 days follow up Second dose	mm (SD)			
	Size of swelling mm (SD)	0	0	N/A
	Size of haematoma mm (SD)	0	0	N/A
	Size of granuloma mm (SD)	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 30 days follow up Second dose	Pain	2	1	0.570 ***
	Redness	0	0	N/A
	Swelling	0	0	N/A
	Heat	0	0	N/A
	Granulomas	1	0	0.573 ***
	Haematoma	0	0	N/A
	Axillary node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 30 day follow up Second dose	Pain intensity (scale 1 to 10)	0.14 (0.351)	0.05 (0.23)	0.353 *
	Redness size mm (SD)	0	0	N/A
	Size of swelling mm (SD)	0	0	N/A
	Size of haematoma mm (SD)	0	0	N/A
	Size of granuloma mm (SD)	0.364 (1.7)	0	0.353*
Increase of the brachial perimeter mm Mean (SD) 1 day follow up second dose		4.81 (14.7)	6.1 (7.1)	0.04 *
Increase of the brachial perimeter mm Mean (SD) 2 days follow up second dose		4.3 (9.41)	3.75 (6.7)	0.711 *
Increase of the brachial perimeter mm Mean (SD) 14 days follow up second dose		2.04 (3.98)	2.65 (5.27)	0.886 *

Increase of the brachial perimeter mm Mean (SD) 30 days follow up second dose		4.1 (12.89)	1.57 (4.1)	0.971 *
Emergence of general symptom (number of cases) 1 day follow up Second dose	Fever	0	0	N/A
	Malaise	0	1	0.476 ***
	Headache	1	1	0.732 ***
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
Emergence of general symptom (number of cases) 2 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	1	0	0.524 ***
	Weakness	1	0	0.524 ***
	Arthralgias	0	0	N/A
Emergence of general symptom (number of cases) 14 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	0	0	N/A
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
Emergence of general symptom (number of cases) 30 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	0	0	N/A
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A

* Mann–Whitney U test (does not fit the normal distribution) ** Chi-squared test *** Fisher's exact test **** Student's-t test (normal distribution) N/A not applicable			
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Third dose of vaccine		Intramuscular group (n = 10)	Subcutaneous group (n = 5)	P value
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 1 day follow up Third dose	Pain	1	4	0.179 ***
	Redness	2	3	0.5 ***
	Swelling	0	2	0.24 ***
	Heat	1	0	0.5 ***
	Granulomas	0	0	N/A
	Haematoma	0	0	N/A
	Axillary node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 1 day follow up Second dose	Pain intensity (scale 1 to 10)	0.38 (0.506)	0.69 (0.95)	0.501 *
	Redness size mm (SD)	1.15 (2.99)	2.46 (5.95)	0.602 *
	Size of swelling mm (SD)	0	2 (5.66)	0.149 *
	Size of haematoma mm (SD)	0	0	N/A
	Size of granuloma mm (SD)	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (number of cases)	Pain	1	2	0.5 ***
	Redness	1	3	0.338 ***
	Swelling	3	2	0.427 ***

2 days follow up Second dose	Heat	2	3	0.538 ***
	Granulomas	0	0	N/A
	Haematoma	0	0	N/A
	Axillary node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 2 days follow up Second dose	Pain intensity (scale 1 to 10)	0.46 (0.66)	0.29 (0.47)	0.902 *
	Redness size mm (SD)	2.08 (5.83)	16.71 (33.7)	0.285 *
	Size of swelling mm (SD)	0.846 (1.86)	15 (38.58)	0.841 *
	Size of haematoma mm (SD)	0	0	N/A
	Size of granuloma mm (SD)	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 14 days follow up Second dose	Pain	2	1	0.576 ***
	Redness	0	1	0.519 ***
	Swelling	0	0	N/A
	Heat	0	0	N/A
	Granulomas	0	0	N/A
	Haematoma	0	0	N/A
	Axillary Node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 14 days follow up Second dose	Pain intensity (scale 1 to 10)	0.23 (0.439)	0.07 (0.267)	0.055 *
	Redness size mm (SD)	0	0.071 (0.267)	0.335 *
	Size of swelling mm (SD)	0	0	N/A
	Size of haematoma mm (SD)	0	0	N/A

	Size of granuloma mm (SD)	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 30 days follow up Second dose	Pain	0	0	N/A
	Redness	0	0	N/A
	Swelling	0	0	N/A
	Heat	0	0	N/A
	Granulomas	0	0	N/A
	Haematoma	0	0	N/A
	Axillary Node	0	0	N/A
Appearance of basic injuries in the area of administration of the vaccine (intensity) 30 days follow up Second dose	Pain intensity (scale 1 to 10)	0	0	N/A
	Redness size mm (SD)	0	0	N/A
	Size of swelling mm (SD)	0	0	N/A
	Size of haematoma mm (SD)	0	0	N/A
	Size of granuloma mm (SD)	0	0	N/A
Increase of the brachial perimeter mm Mean (SD) 1 day follow up second dose		0.38 (1.39)	1.92 (3.83)	0.479 *
Increase of the brachial perimeter mm Mean (SD) 2 days follow up second dose		0.69 (1.7)	3.84 (6.17)	0.243 *
Increase of the brachial perimeter mm Mean (SD) 14 days follow up second dose		0.15 (0.55)	1.15 (2.99)	0.724 *
Increase of the brachial perimeter mm Mean (SD) 30 days follow up second dose		0.16 (0.58)	1.92 (3.83)	0.503 *
Emergence of general symptom (number of cases) 1 day follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	0	0	N/A

	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
Emergence of general symptom (number of cases) 2 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	0	0	N/A
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
Emergence of general symptom (number of cases) 14 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	0	0	N/A
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
Emergence of general symptom (number of cases) 30 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	0	0	N/A
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
* Mann–Whitney U test (does not fit the normal distribution) ** Chi-squared test *** Fisher's exact test **** Student's-t test (normal distribution) N/A not applicable				

Total number of vaccines (inoculations)		Intramuscular group (n doses = 142)	Subcutaneous group (n doses = 147)	P value
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 1 day follow up Third dose	Pain	45	37	0.219 ***
		59	46	0.072 ***
	Redness	8	29	0.001 ***
				0.001 **
	Swelling	9	27	0.002 ***
		9	24	0.007 **
	Heat	11	20	0.108 ***
				0.064 ***
	Granulomas	9	8	0.746 ***
		2	4	0.342 ***
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 2 day follow up Second dose	Haematoma	3	5	0.504 ***
				0.361 ***
	Axillary node	0	0	N/A
	Pain	37	33	0.234 ***
		34	28	
	Redness	12	29	0.080 ***
		21	31	
	Swelling	14	30	0.005 ***
		13	29	
	Heat	14	22	0.066 ***
		16	26	
	Granulomas	7	8	0.107 ***

		1	5	
	Haematoma	1	3	0.141 ***
		5	10	
	Axillary node	0	1	
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 14 day follow up Second dose	Pain	9	9	0.056 ***
		18	9	
	Redness	8	5	0.286 ***
	Swelling	1	3	0.306 ***
	Heat	1	1	0.747 ***
	Granulomas	1	2	0.495 ***
	Haematoma	1	0	0.503 ***
Appearance of basic injuries in the area of administration of the vaccine (number of cases) 30 day follow up Second dose	Pain	3	3	0.504 ***
		4	5	
	Redness	2	1	0.495 ***
	Swelling	0	0	N/A
	Heat	0	0	N/A
	Granulomas	01	1	0.503 ***
	Haematoma	0	0	N/A
Emergence of general symptom (number of cases) 1 day follow up Second dose	Fever	3	2	0.497 ***
	Malaise	8	3	0.107 ***
	Headache	5	2	0.221 ***
	Weakness	3	1	0.309 ***
	Arthralgias	1	0	0.498 ***

Emergence of general symptom (number of cases) 2 days follow up Second dose	Fever	3	4	0.504 ***
	Malaise	6	1	0.059 ***
	Headache	3	1	0.309 ***
	Weakness	5	0	0.030 ***
	Arthralgias	2	0	0.247 ***
Emergence of general symptom (number of cases) 14 days follow up Second dose	Fever	0	1	0.498 ***
	Malaise	0	0	N/A
	Headache	1	2	0.497 ***
	Weakness	1	0	0.502 ***
	Arthralgias	0	1	0.498 ***
Emergence of general symptom (number of cases) 30 days follow up Second dose	Fever	0	0	N/A
	Malaise	0	0	N/A
	Headache	1	0	0.497 ***
	Weakness	0	0	N/A
	Arthralgias	0	0	N/A
* Mann–Whitney U test (does not fit the normal distribution) ** Chi-squared test *** Fisher's exact test **** Student's-t test (normal distribution) N/A not applicable				