

## Supplementary Materials

**Supplementary Table 1. Demographics for participants included in the efficacy analysis**

<b>Variable</b>	<b>Overall n = 1,895</b>	<b>Placebo N = 960</b>	<b>Vaccine N = 935</b>
Male, n (%)	1,047 (55.3)	520 (54.2)	527 (56.4)
HIV positive, n (%)	98 (5.2)	48 (5)	50 (5.3)
Median Age, years (IQR)	31 (25–41)	31 (25–40)	31 (25–41)
18–< 45	1,568 (82.7)	798 (83.1)	770 (82.4)
45–< 60	288 (15.2)	139 (14.5)	149 (15.9)
≥ 60	39 (2.1)	23 (2.4)	16 (1.7)
BMI, n (%)			
Underweight	148 (7.8)	66 (6.9)	82 (8.8)
Normal	942 (49.8)	483 (50.3)	459 (49.2)
Overweight	433 (22.9)	209 (21.8)	224 (24)
Obese	370 (19.5)	202 (21)	168 (18)
Smoker, n (%)	808 (42.6)	394 (41)	414 (44.3)
Alcohol, n (%)	931 (49.1)	469 (48.9)	462 (49.4)
Health worker, n (%)	157 (8.3)	87 (9.1)	70 (7.5)
Race, n (%)			
Black	1,330 (70.3)	674 (70.4)	656 (70.2)
Mixed	281 (14.9)	138 (14.4)	143 (15.3)
White	244 (12.9)	128 (13.4)	116 (12.4)
Other	36 (1.9)	17 (1.8)	19 (2)
Complications, n (%)	143 (7.5)	68 (7.1)	75 (8)
Hypertension	67 (3.5)	33 (3.4)	34 (3.6)
Respiratory system	73 (3.9)	33 (3.4)	40 (4.3)

Diabetes	8 (0.4)	4 (0.4)	4 (0.4)
Time between doses, median days (IQR)	28 (28–32)	28 (28–32)	28 (28–32)
Follow-up time, median days (IQR) <sup>a</sup>	250 (216–298)	251 (219–301)	249 (213–291)
Total follow-up time, per person-days <sup>a</sup>	480,697	244,140	236,557

<sup>a</sup>Follow-up time was calculated as the time from 2<sup>nd</sup> injection to first of the following events: withdrawal, death, SARS-CoV-2 infection, unblinding or censored by 15 November 2021. Abbreviations: BMI, Body mass index; IQR, Interquartile range.

**Supplementary Table 2. Variant distribution by severity**

Severity	Total cases	WT	Beta	Delta	Failed library	
					preparation <sup>†</sup>	Unclassified <sup>‡</sup>
<b>Any infection*</b>	171 <sup>†</sup>	12	99	22	8	30
Placebo	107	11	52	18	6	20
Vaccine	64	1	47	4	2	10
<b>Mild/Moderate</b>	124	10	70	21	5	18
Placebo	81	9	37	17	5	13
Vaccine	43	1	33	4	0	5
<b>Moderate</b>	45	7	27	5	2	4
Placebo	27	6	13	4	2	2
Vaccine	18	1	14	1	0	2

\*Includes symptomatic and asymptomatic infections.

<sup>†</sup>One severe case happened after unblinding.

<sup>‡</sup>See Supplementary Table S4 for further details.

Specimens with a cycle threshold >35 tended to fail library preparation and were not sequenced, while samples with a cycle threshold between 32–35 tended to have poor genome coverage and we were unable to determine their SARS-CoV-2 classification. Abbreviation: WT, Wild type.

**Supplementary Table 3. Distribution of samples that were unclassified for SARS-CoV-2 variant or failed library preparation**

	Pre-October 2020		October 2020 to April 2021		May to November 2021			
	Failed library preparation	Unclassified	Failed library preparation	Unclassified	Failed library preparation	Unclassified	Failed library preparation	Unclassified
<b>Any infection</b>	8	30	0	1	7	26	1	3
Placebo	6	20	0	1	5	16	1	3
Vaccine	2	10	0	0	2	10	0	0
<b>Mild/Moderate</b>	5	18	0	1	4	15	1	2
Placebo	5	13	0	1	4	10	1	2
Vaccine	0	5	0	0	0	5	0	0
<b>Moderate</b>	2	4	0	0	1	4	1	0
Placebo	2	2	0	0	1	2	1	0
Vaccine	0	2	0	0	0	2	0	0

**Supplementary Table 4. Vaccine efficacy sensitivity analysis.** This table includes infections where the variant was unclassifiable. Infections pre-October 2020 were assigned a wild type classification, between October 2020–April 2021 were assigned Beta classification and between May–November 2021 were assigned Delta classification.

Severity	SARS-CoV-2	Total cases	Placebo n = 960			Vaccine n = 935			VE (95% CI)
			Total FU time (days) = 244,140			Total FU time (days) = 236,557			
			Mean FU in days (SD) = 254 (71)			Mean FU in days (SD) = 253 (74)			
						Incidence			
			Mean FU in months n (%)	Incidence rate (person- days) (SD)		Mean FU in months n (%)	Incidence rate (person- days) (SD)		
<b>Any infection*</b>	WT	13	12 (1.2)	4.3 (3.1)	17.9	1 (0.1)	0.6 (2.2)	1.5	91.4% (41.9, 99.8)
	Beta	132	73 (7.6)	4.5 (1.5)	109.1	59 (6.3)	4.2 (NA)	91.0	16.6% (-19.2, 41.8)
	Delta	26	22 (2.3)	9.5 (1.2)	32.9	4 (0.4)	10 (0.7)	6.2	81.2% (44.7, 95.3)
<b>Mild/ Moderate</b>	WT	11	10 (1)	4.2 (3.4)	15	1 (0.1)	0.6 (NA)	1.5	89.7% (27.5, 99.8)
	Beta	89	51 (5.3)	4.4 (1.6)	76.2	38 (4.1)	3.9 (1.8)	58.6	23.1% (-19.4, 50.8)
	Delta	24	20 (2.1)	9.6 (1.0)	29.9	4 (0.4)	10 (0.7)	6.2	79.4% (38.4, 94.9)

\*Includes symptomatic and asymptomatic infections. Abbreviations: CI, Confidence interval; FU, Follow-up; NA, Not applicable; SD, Standard deviation; VE, Vaccine efficacy; WT, Wild type.

**Supplementary Table 5. Summary of adverse events by system organ class and high-level preferred term**

<b>N (%)</b>	<b>Overall</b>	<b>Placebo</b>	<b>Vaccine</b>
Any adverse event	4,640	2,329	2,311
General disorders and administration site conditions	1,756 (82.6)	836 (78.7)	920 (86.5)
General system disorders NEC	1,634 (76.9)	795 (74.9)	839 (78.9)
Administration site reactions	77 (3.6)	23 (2.2)	54 (5.1)
Body temperature conditions	42 (2)	16 (1.5)	26 (2.4)
Therapeutic and nontherapeutic effects (excl toxicity)	2 (<0.1)	1 (<0.1)	1 (<0.1)
Tissue disorders NEC	1 (<0.1)	1 (<0.1)	0 (<0.1)
Eye disorders	37 (1.7)	21 (2)	16 (1.5)
Ocular infections, irritations and inflammations	33 (1.6)	20 (1.9)	13 (1.2)
Eye disorders NEC	3 (0.1)	1 (<0.1)	2 (0.2)
Vision disorders	1 (<0.1)	0 (<0.1)	1 (<0.1)
Metabolism and nutrition disorders	33 (1.6)	15 (1.4)	18 (1.7)
Appetite and general nutritional disorders	19 (0.9)	8 (0.8)	11 (1)
Electrolyte and fluid balance conditions	8 (0.4)	4 (0.4)	4 (0.4)
Glucose metabolism disorders (incl diabetes mellitus)	4 (0.2)	1 (<0.1)	3 (0.3)
Bone, calcium, magnesium and phosphorus metabolism disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
Purine and pyrimidine metabolism disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
Injury, poisoning and procedural complications	30 (1.4)	13 (1.2)	17 (1.6)
Injuries NEC	21 (1)	9 (0.8)	12 (1.1)
Injuries by physical agents	4 (0.2)	2 (0.2)	2 (0.2)
Bone and joint injuries	3 (0.1)	1 (<0.1)	2 (0.2)
Procedural related injuries and complications NEC	2 (<0.1)	1 (<0.1)	1 (<0.1)

Reproductive system and breast disorders	25 (1.2)	11 (1)	14 (1.3)
Menstrual cycle and uterine bleeding disorders	16 (0.8)	10 (0.9)	6 (0.6)
Sexual function and fertility disorders	4 (0.2)	0 (<0.1)	4 (0.4)
Reproductive tract disorders NEC	2 (<0.1)	1 (<0.1)	1 (<0.1)
Vulvovaginal disorders (excl infections and inflammations)	2 (<0.1)	0 (<0.1)	2 (0.2)
Uterine, pelvic and broad ligament disorders	1 (<0.1)	0 (<0.1)	1 (<0.1)
Blood and lymphatic system disorders	12 (0.6)	6 (0.6)	6 (0.6)
Anemias nonhemolytic and marrow depression	5 (0.2)	2 (0.2)	3 (0.3)
Spleen, lymphatic and reticuloendothelial system disorders	5 (0.2)	4 (0.4)	1 (<0.1)
Red blood cell disorders	2 (<0.1)	0 (<0.1)	2 (0.2)
Ear and labyrinth disorders	8 (0.4)	2 (0.2)	6 (0.6)
Aural disorders NEC	7 (0.3)	2 (0.2)	5 (0.5)
External ear disorders (excl congenital)	1 (<0.1)	0 (<0.1)	1 (<0.1)
Cardiac disorders	6 (0.3)	3 (0.3)	3 (0.3)
Cardiac arrhythmias	3 (0.1)	1 (<0.1)	2 (0.2)
Cardiac disorders, signs and symptoms NEC	3 (0.1)	2 (0.2)	1 (<0.1)
Psychiatric disorders	6 (0.3)	5 (0.5)	1 (<0.1)
Anxiety disorders and symptoms	2 (<0.1)	2 (0.2)	0 (<0.1)
Depressed mood disorders and disturbances	2 (<0.1)	1 (<0.1)	1 (<0.1)
Schizophrenia and other psychotic disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
Sleep disorders and disturbances	1 (<0.1)	1 (<0.1)	0 (<0.1)
Renal and urinary disorders	5 (0.2)	2 (0.2)	3 (0.3)
Urinary tract signs and symptoms	4 (0.2)	1 (<0.1)	3 (0.3)
Urolithiases	1 (<0.1)	1 (<0.1)	0 (<0.1)
Immune system disorders	4 (0.2)	3 (0.3)	1 (<0.1)
Allergic conditions	4 (0.2)	3 (0.3)	1 (<0.1)
Respiratory, thoracic and mediastinal disorders	681 (32)	351 (33.1)	330 (31)

Respiratory disorders NEC	332 (15.6)	173 (16.3)	159 (15)
Respiratory tract signs and symptoms	266 (12.5)	132 (12.4)	134 (12.6)
Upper respiratory tract disorders (excl infections)	78 (3.7)	44 (4.1)	34 (3.2)
Pulmonary vascular disorders	3 (0.1)	2 (0.2)	1 (<0.1)
Bronchial disorders (excl neoplasms)	2 (<0.1)	0 (<0.1)	2 (0.2)
Endocrine disorders	3 (0.1)	3 (0.3)	0 (<0.1)
Thyroid gland disorders	3 (0.1)	3 (0.3)	0 (<0.1)
Hepatobiliary disorders	3 (0.1)	3 (0.3)	0 (<0.1)
Hepatic and hepatobiliary disorders	3 (0.1)	3 (0.3)	0 (<0.1)
Social circumstances	3 (0.1)	1 (<0.1)	2 (0.2)
Legal issues	3 (0.1)	1 (<0.1)	2 (0.2)
Pregnancy, puerperium and perinatal conditions	2 (<0.1)	1 (<0.1)	1 (<0.1)
Abortions and stillbirth	2 (<0.1)	1 (<0.1)	1 (<0.1)
Nervous system disorders	654 (30.8)	336 (31.6)	318 (29.9)
Headaches	489 (23)	253 (23.8)	236 (22.2)
Neurological disorders NEC	101 (4.8)	54 (5.1)	47 (4.4)
Cranial nerve disorders (excl neoplasms)	63 (3)	28 (2.6)	35 (3.3)
Peripheral neuropathies	1 (<0.1)	1 (<0.1)	0 (<0.1)
Infections and infestations	559 (26.3)	276 (26)	283 (26.6)
Infections – pathogen unspecified	468 (22)	229 (21.6)	239 (22.5)
Viral infectious disorders	67 (3.2)	36 (3.4)	31 (2.9)
Fungal infectious disorders	11 (0.5)	5 (0.5)	6 (0.6)
Bacterial infectious disorders	10 (0.5)	3 (0.3)	7 (0.7)
Ectoparasitic disorders	2 (<0.1)	2 (0.2)	0 (<0.1)
Helminthic disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
Gastrointestinal disorders	469 (22.1)	243 (22.9)	226 (21.3)
Gastrointestinal motility and defaecation conditions	232 (10.9)	117 (11)	115 (10.8)



Gastrointestinal signs and symptoms	217 (10.2)	118 (11.1)	99 (9.3)
Dental and gingival conditions	7 (0.3)	5 (0.5)	2 (0.2)
Oral soft tissue conditions	7 (0.3)	2 (0.2)	5 (0.5)
Gastrointestinal vascular conditions	3 (0.1)	1 (<0.1)	2 (0.2)
Gastrointestinal hemorrhages NEC	1 (<0.1)	0 (<0.1)	1 (<0.1)
Gastrointestinal inflammatory conditions	1 (<0.1)	0 (<0.1)	1 (<0.1)
Gastrointestinal ulceration and perforation	1 (<0.1)	0 (<0.1)	1 (<0.1)
<b>Musculoskeletal and connective tissue disorders</b>	<b>163 (7.7)</b>	<b>102 (9.6)</b>	<b>61 (5.7)</b>
Muscle disorders	63 (3)	44 (4.1)	19 (1.8)
Musculoskeletal and connective tissue disorders NEC	53 (2.5)	28 (2.6)	25 (2.4)
Joint disorders	45 (2.1)	28 (2.6)	17 (1.6)
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	1 (<0.1)	1 (<0.1)	0 (<0.1)
Tendon, ligament and cartilage disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
<b>Skin and subcutaneous tissue disorders</b>	<b>73 (3.4)</b>	<b>54 (5.1)</b>	<b>19 (1.8)</b>
Epidermal and dermal conditions	43 (2)	33 (3.1)	10 (0.9)
Skin appendage conditions	27 (1.3)	20 (1.9)	7 (0.7)
Angioedema and urticaria	3 (0.1)	1 (<0.1)	2 (0.2)
<b>Investigations</b>	<b>65 (3.1)</b>	<b>22 (2.1)</b>	<b>43 (4)</b>
Cardiac and vascular investigations (excl enzyme tests)	37 (1.7)	11 (1)	26 (2.4)
Physical examination and organ system status topics	8 (0.4)	1 (<0.1)	7 (0.7)
Water, electrolyte and mineral investigations	8 (0.4)	5 (0.5)	3 (0.3)
Hepatobiliary investigations	5 (0.2)	3 (0.3)	2 (0.2)
Hematology investigations (incl blood groups)	3 (0.1)	1 (<0.1)	2 (0.2)
Enzyme investigations NEC	2 (<0.1)	1 (<0.1)	1 (<0.1)
Metabolic, nutritional and blood gas investigations	1 (<0.1)	0 (<0.1)	1 (<0.1)
Microbiology and serology investigations	1 (<0.1)	0 (<0.1)	1 (<0.1)

Vascular disorders	43 (2)	20 (1.9)	23 (2.2)
Vascular hypertensive disorders	40 (1.9)	18 (1.7)	22 (2.1)
Decreased and nonspecific blood pressure disorders and shock	2 (<0.1)	1 (<0.1)	1 (<0.1)
Embolism and thrombosis	1 (<0.1)	1 (<0.1)	0 (<0.1)

Abbreviation: NEC, Not elsewhere classified.

**Supplementary Table 6. Summary of serious adverse events by system organ class and high-level preferred term**

<b>N (%)</b>	<b>Overall</b>	<b>Placebo</b>	<b>Vaccine</b>
Any serious adverse event	58	24	34
Injury, poisoning and procedural complications	13 (0.6)	4 (0.4)	9 (0.8)
Injuries NEC	7 (0.3)	2 (0.2)	5 (0.5)
Bone and joint injuries	4 (0.2)	1 (<0.1)	3 (0.3)
Overdoses and underdoses NEC	1 (<0.1)	0 (<0.1)	1 (<0.1)
Procedural related injuries and complications NEC	1 (<0.1)	1 (<0.1)	0 (<0.1)
Hepatobiliary disorders	2 (<0.1)	2 (0.2)	0 (<0.1)
Hepatic and hepatobiliary disorders	2 (<0.1)	2 (0.2)	0 (<0.1)
Social circumstances	2 (<0.1)	1 (<0.1)	1 (<0.1)
Legal issues	2 (<0.1)	1 (<0.1)	1 (<0.1)
Immune system disorders	1 (<0.1)	0 (<0.1)	1 (<0.1)
Allergic conditions	1 (<0.1)	0 (<0.1)	1 (<0.1)
Investigations	1 (<0.1)	1 (<0.1)	0 (<0.1)
Hepatobiliary investigations	1 (<0.1)	1 (<0.1)	0 (<0.1)
Musculoskeletal and connective tissue disorders	1 (<0.1)	0 (<0.1)	1 (<0.1)
Fractures	1 (<0.1)	0 (<0.1)	1 (<0.1)
Nervous system disorders	1 (<0.1)	0 (<0.1)	1 (<0.1)
Neurological disorders NEC	1 (<0.1)	0 (<0.1)	1 (<0.1)
Reproductive system and breast disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
Menstrual cycle and uterine bleeding disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
Gastrointestinal disorders	7 (0.3)	3 (0.3)	4 (0.4)
Exocrine pancreas conditions	2 (<0.1)	0 (<0.1)	2 (0.2)
Gastrointestinal inflammatory conditions	2 (<0.1)	1 (<0.1)	1 (<0.1)
Gastrointestinal conditions NEC	1 (<0.1)	1 (<0.1)	0 (<0.1)

Gastrointestinal motility and defecation conditions	1 (<0.1)	1 (<0.1)	0 (<0.1)
Gastrointestinal stenosis and obstruction	1 (<0.1)	0 (<0.1)	1 (<0.1)
<b>Infections and infestations</b>	<b>7 (0.3)</b>	<b>3 (0.3)</b>	<b>4 (0.4)</b>
Infections – pathogen unspecified	3 (0.1)	2 (0.2)	1 (<0.1)
Mycobacterial infectious disorders	2 (<0.1)	0 (<0.1)	2 (0.2)
Bacterial infectious disorders	1 (<0.1)	0 (<0.1)	1 (<0.1)
Viral infectious disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
<b>Pregnancy, puerperium and perinatal conditions</b>	<b>6 (0.3)</b>	<b>1 (&lt;0.1)</b>	<b>5 (0.5)</b>
Abortions and stillbirth	4 (0.2)	1 (<0.1)	3 (0.3)
Maternal complications of pregnancy	2 (<0.1)	0 (<0.1)	2 (0.2)
<b>General disorders and administration site conditions</b>	<b>4 (0.2)</b>	<b>0 (&lt;0.1)</b>	<b>4 (0.4)</b>
Body temperature conditions	2 (<0.1)	0 (<0.1)	2 (0.2)
General system disorders NEC	2 (<0.1)	0 (<0.1)	2 (0.2)
<b>Psychiatric disorders</b>	<b>4 (0.2)</b>	<b>2 (0.2)</b>	<b>2 (0.2)</b>
Schizophrenia and other psychotic disorders	2 (<0.1)	1 (<0.1)	1 (<0.1)
Suicidal and self-injurious behaviors NEC	2 (<0.1)	1 (<0.1)	1 (<0.1)
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>4 (0.2)</b>	<b>3 (0.3)</b>	<b>1 (&lt;0.1)</b>
Pulmonary vascular disorders	3 (0.1)	2 (0.2)	1 (<0.1)
Pleural disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)
<b>Blood and lymphatic system disorders</b>	<b>2 (&lt;0.1)</b>	<b>1 (&lt;0.1)</b>	<b>1 (&lt;0.1)</b>
Anemias nonhemolytic and marrow depression	2 (<0.1)	1 (<0.1)	1 (<0.1)
<b>Cardiac disorders</b>	<b>2 (&lt;0.1)</b>	<b>2 (0.2)</b>	<b>0 (&lt;0.1)</b>
Cardiac disorders, signs and symptoms NEC	1 (<0.1)	1 (<0.1)	0 (<0.1)
Coronary artery disorders	1 (<0.1)	1 (<0.1)	0 (<0.1)

Abbreviation: NEC, Not elsewhere classified.