Online Data Supplement
Safety and Reactogenicity of Coronavirus Disease 2019 Vaccination in Severe Alpha-1 Antitrypsin Deficiency

Oliver J. McElvaney, MD, PhD[1,2,3,4] Brian Cleary, MD[1] Daniel D. Fraughen, MD[1,2] Geraldine Kelly, MBA[5] Oisin F. McElvaney, MD, PhD[1] Mark P. Murphy, PhD[1] Peter Branagan, MD[1,2] Cedric Gunaratnam, MD[1,2] Tomás P. Carroll, PhD[1,5] Christopher H. Goss, MD, MSc[3,4,6] Noel G. McElvaney, MD[1,2]

[1] Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

[2] National Centre for Alpha-1 Antitrypsin Deficiency, Beaumont Hospital, Dublin, Ireland

[3] Seattle Children's Research Institute, Seattle, Washington, United States

[4] Department of Medicine, University of Washington, Seattle, Washington, United States
[5] Alpha-1 Foundation of Ireland, Dublin, Ireland

[6] Department of Pediatrics, University of Washington, Seattle, Washington, United States

Supplementary appendix AATD

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Table S1. Baseline clinical characteristics of the Pi*MM COPD study cohort	
Number	150
Male	71 (47)
Female	79 (53)
Age (years)	66.1 ± 12.4
Current smokers	69 (46)
Never-smokers	0 (0)
Ex-smokers	81 (54)
Vapers	14 (9)
FEV_1 (% predicted)	57.5 ± 22.6
DLCO (% predicted)*	53.2 ± 20.9
Supplemental oxygen	13 (9)

Data are presented as number (%) or mean ± standard deviation.
* Data available for n = 142
FEV_1 – forced expiratory volume in 1s
DLCO = diffusing capacity for carbon monoxide

Table S2. Breakdown of study groups by age and sex			
	NLD	**Pi*MM COPD**	**Pi*ZZ AATD**
Total number	140	150	170
<50 years	70	NA	81
Male	36	NA	41
Female	34	NA	40
≥50 years	70	150	89
Male	35	71	45
Female	35	79	44

Data presented as absolute number
NLD – non-lung disease control group
COPD – chronic obstructive pulmonary disease
AATD – alpha-1 antitrypsin deficiency

Table S3. Burden of comorbid disease in the study cohort			
	NLD (n=140)	**Pi*MM COPD (n=150)**	**Pi*ZZ AATD (n=170)**
Hypertension	50 (36)	63 (42)	64 (38)
Coronary artery disease	22 (16)	27 (18)	23 (14)
Diabetes mellitus	14 (10)	19 (13)	18 (11)
Obesity	29 (21)	36 (24)	31 (18)
Chronic kidney disease	22 (16)	19 (13)	17 (10)
Vasculitis or connective tissue disease	4 (3)	3 (2)	5 (3)
Neurodegenerative disease	0 (0)	1 (1)	0 (0)
Chronic liver disease	4 (3)	7 (5)	39 (23)
Inflammatory bowel disease	1 (1)	1 (1)	0 (0)
Solid organ malignancy	2 (1)	1 (1)	0 (0)
Depression	5 (4)	10 (7)	7 (4)
Prior VTE	2 (1)	3 (2)	2 (1)

Data presented as number (%)
NLD – non-lung disease control group
COPD – chronic obstructive pulmonary disease
AATD – alpha-1 antitrypsin deficiency
VTE – venous thromboembolism

Table S4. Relative risk of COVID-19 vaccine-associated events in Pi*ZZ AATD patients compared to non-lung disease controls

	1st dose (n=140)		2nd dose (n=136)	
Local	RR (95% CI)	p-value	RR (95% CI)	p-value
Pain	1.02 (0.82 – 1.26)	0.89	0.89 (0.67 – 1.18)	0.42
Mild	1.08 (0.80 – 1.45)	0.63	0.96 (0.68 – 1.36)	0.83
Moderate	0.90 (0.52 – 1.56)	0.71	0.69 (0.33 – 1.44)	0.32
Severe	0.82 (0.17 – 4.02)	0.81	0.80 (0.05 – 12.74)	0.88
Swelling	0.82 (0.41 – 1.67)	0.60	0.89 (0.37 – 2.14)	0.80
Tenderness	0.97 (0.87 – 1.08)	0.57	0.91 (0.80 – 1.05)	0.19
Pruritis	0.74 (0.31 – 1.77)	0.50	1.34 (0.33 – 5.51)	0.68
Axillary LA	1.37 (0.33 – 5.64)	0.66	4.02 (0.48 – 34.03)	0.16
Erythema	0.90 (0.41 – 1.97)	0.79	1.29 (0.43 – 3.85)	0.65
Warmth	0.70 (0.38 – 1.28)	0.25	0.57 (0.26 – 1.25)	0.16
Bruising	0.82 (0.32 – 2.14)	0.69	0.80 (0.24 – 2.72)	0.73
Fatigue	1.05 (0.84 – 1.32)	0.65	1.16 (0.90 – 1.50)	0.24
Headache	1.04 (0.86 – 1.25)	0.70	0.98 (0.77 – 1.24)	0.86
Arthralgia	1.06 (0.74 – 1.52)	0.74	1.36 (0.81 – 2.28)	0.25
Myalgia	0.79 (0.49 – 1.29)	0.35	1.15 (0.60 – 2.19)	0.67
Nausea	0.70 (0.38 – 1.28)	0.25	0.91 (0.47 – 1.76)	0.78
Fever	0.95 (0.63 – 1.44)	0.82	0.91 (0.54 – 1.55)	0.74
Chills/rigors	1.08 (0.77 – 1.52)	0.64	0.91 (0.47 – 1.76)	0.78
Less common				
Anorexia	0.99 (0.44 – 2.22)	0.98	1.13 (0.37 – 3.47)	0.84
Diarrhea	0.55 (0.09 – 3.24)	0.50	0.54 (0.09 – 3.17)	0.48
Vomiting	0.82 (0.17 – 4.02)	0.81	NA	0.20
Dizziness	1.18 (0.46 – 3.01)	0.73	0.80 (0.24 – 2.72)	0.73
Sweating	0.82 (0.30 – 2.29)	0.71	1.29 (0.43 – 3.85)	0.65
Generalized LA	0.82 (0.05 – 13.05)	0.89	0.80 (0.11 – 5.64)	0.83
Any local	0.98 (0.88 – 1.09)	0.70	0.96 (0.85 – 1.08)	0.50
Any systemic	0.95 (0.80 – 1.13)	0.59	0.97 (0.78 – 1.19)	0.74
Symptoms >3d	1.08 (0.77 – 1.51)	0.66	0.91 (0.47 – 1.76)	0.78
Symptoms >5d	0.90 (0.41 – 1.97)	0.79	2.41 (0.25 – 22.95)	0.43

LA – lymphadenopathy

Table S5. Relative risk of COVID-19 vaccine-associated events in Pi*ZZ AATD patients compared to Pi*MM COPD controls

	1st dose (n=140)		2nd dose (n=136)	
Local	RR (95% CI)	p-value	RR (95% CI)	p-value
Pain	1.09 (0.88 – 1.35)	0.45	1.04 (0.77 – 1.39)	0.81
Mild	1.25 (0.92 – 1.71)	0.15	1.04 (0.73 – 1.48)	0.83
Moderate	0.78 (0.47 – 1.31)	0.35	0.95 (0.43 – 2.09)	0.90
Severe	1.32 (0.22 – 7.81)	0.76	NA	0.35
Swelling	0.95 (0.46 – 1.96)	0.89	0.87 (0.37 – 2.03)	0.75
Tenderness	1.03 (0.92 – 1.17)	0.55	0.97 (0.84 – 1.12)	0.66
Pruritis	1.32 (0.48 – 3.63)	0.58	NA	**0.04**
Axillary LA	1.47 (0.36 – 6.05)	0.59	1.45 (0.35 – 5.96)	0.60
Erythema	1.18 (0.51 – 2.71)	0.70	0.77 (0.31 – 1.95)	0.59
Warmth	0.88 (0.47 – 1.67)	0.70	0.58 (0.29 – 1.25)	0.16
Bruising	1.41 (0.47 – 4.22)	0.53	0.72 (0.23 – 2.34)	0.59
Fatigue	1.16 (0.92 – 1.47)	0.20	1.19 (0.93 – 1.54)	0.16
Headache	1.08 (0.90 – 1.31)	0.40	0.95 (0.76 – 1.20)	0.69
Arthralgia	1.31 (0.89 – 1.92)	0.16	1.27 (0.77 – 2.08)	0.35
Myalgia	0.96 (0.57 – 1.59)	0.86	1.16 (0.62 – 2.18)	0.65
Nausea	0.83 (0.45 – 1.56)	0.57	1.48 (0.70 – 3.13)	0.30
Fever	1.09 (0.71 – 1.67)	0.70	0.91 (0.54 – 1.52)	0.71
Chills/rigors	1.08 (0.78 – 1.51)	0.64	1.23 (0.61 – 2.49)	0.56
Less common				
Anorexia	1.18 (0.51 – 2.71)	0.70	0.68 (0.26 – 1.77)	0.42
Diarrhea	0.59 (0.10 – 3.47)	0.55	0.60 (0.10 – 3.42)	0.54
Vomiting	0.88 (0.18 – 4.31)	0.88	1.74 (0.16 – 18.99)	0.65
Dizziness	1.47 (0.55 – 3.95)	0.44	1.45 (0.35 – 5.96)	0.60
Sweating	0.77 (0.29 – 2.08)	0.61	1.16 (0.41 – 3.27)	0.78
Generalized LA	0.29 (0.03 – 2.80)	0.26	0.87 (0.12 – 6.10)	0.89
Any local	1.01 (0.91 – 1.13)	0.79	1.01 (0.89 – 1.14)	0.88
Any systemic	1.03 (0.86 – 1.24)	0.73	1.06 (0.85 – 1.31)	0.61
Symptoms >3d	1.18 (0.84 – 1.66)	0.33	0.99 (0.51 – 1.90)	0.97
Symptoms >5d	1.18 (0.51 – 2.71)	0.70	0.87 (0.18 – 4.24)	0.86

LA – lymphadenopathy

Table S6. Unexpected events or AESI following administration of ChAdOx1 nCoV-19						
	NLD		**Pi*MM COPD**		**Pi*ZZ AATD**	
	1st dose (n=140)	2nd dose (n=136)	1st dose (n=150)	2nd dose (n=147)	1st dose (n=170)	2nd dose (n=169)
Seizure	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Collapse	2 (0.7)	0 (0)	1 (0.7)	0 (0)	1 (0.6)	0 (0)
Rash	2 (1.4)	1 (0.7)	2 (1.3)	1 (0.7)	2 (1.2)	0 (0)
Anaphylactoid reaction	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anaphylaxis	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unexplained bleeding	1 (0.7)	0 (0)	1 (0.7)	0 (0)	0 (0)	0 (0)
Unexplained bruising	2 (1.4)	1 (0.7)	0 (0)	2 (1.3)	3 (1.8)	2 (1.2)
VTE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CVST	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Capillary leak syndrome	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Data presented as number (%)
NLD – non-lung disease control group
VTE – venous thromboembolism
CVST – cerebral venous sinus thrombosis

Table S7. Patient-directed event reporting in the study cohort					
Pi*ZZ AATD	**ChAdOx1 nCoV-19**		**BNT162b2**		**Total**
AE descriptor	1st dose	2nd dose	1st booster*	2nd booster†	
Systemic	2/103 [2]	2/90 [2]	1/78 [1]	1/42 [2]	6/313 [2]
Severe‡ or prolonged	4/63 [6]	2/24 [8]	1/32 [3]	0/35 [0]	7/154 [5]
AESI	1/6 [17]	0/2 [0]	NA	NA	1/8 [13]
Pi*MM COPD	**ChAdOx1 nCoV-19**		**BNT162b2**		**Total**
AE descriptor	1st dose	2nd dose	1st booster	2nd booster	
Systemic	2/88 [2]	3/74 [4]	NA	NA	5/162 [3]
Severe‡ or prolonged	4/50 [8]	1/19 [5]	NA	NA	5/69 [7]
AESI	0/4 [0]	0/3 [0]	NA	NA	0/7 [0]
NLD	**ChAdOx1 nCoV-19**		**BNT162b2**		**Total**
AE descriptor	1st dose	2nd dose	1st booster	2nd booster	
Systemic	4/89 [4]	1/75 [1]	NA	NA	5/164 [3]
Severe‡ or prolonged	3/49 [6]	2/19 [11]	NA	NA	5/68 [7]
AESI	0/8 [0]	0/2 [0]	NA	NA	0/10 [0]

Data presented as number who reported an event /total number with an event, [%]
* Monovalent vaccine
† Bivalent vaccine ± quadrivalent influenza vaccine
‡ FDA Toxicity Grading Scale grade III/IV
AATD – alpha-1 antitrypsin deficiency
COPD – chronic obstructive pulmonary disease
NLD – non-lung disease controls
AE – adverse event
AESI – adverse event of special interest
NA – not applicable

Supplementary figures

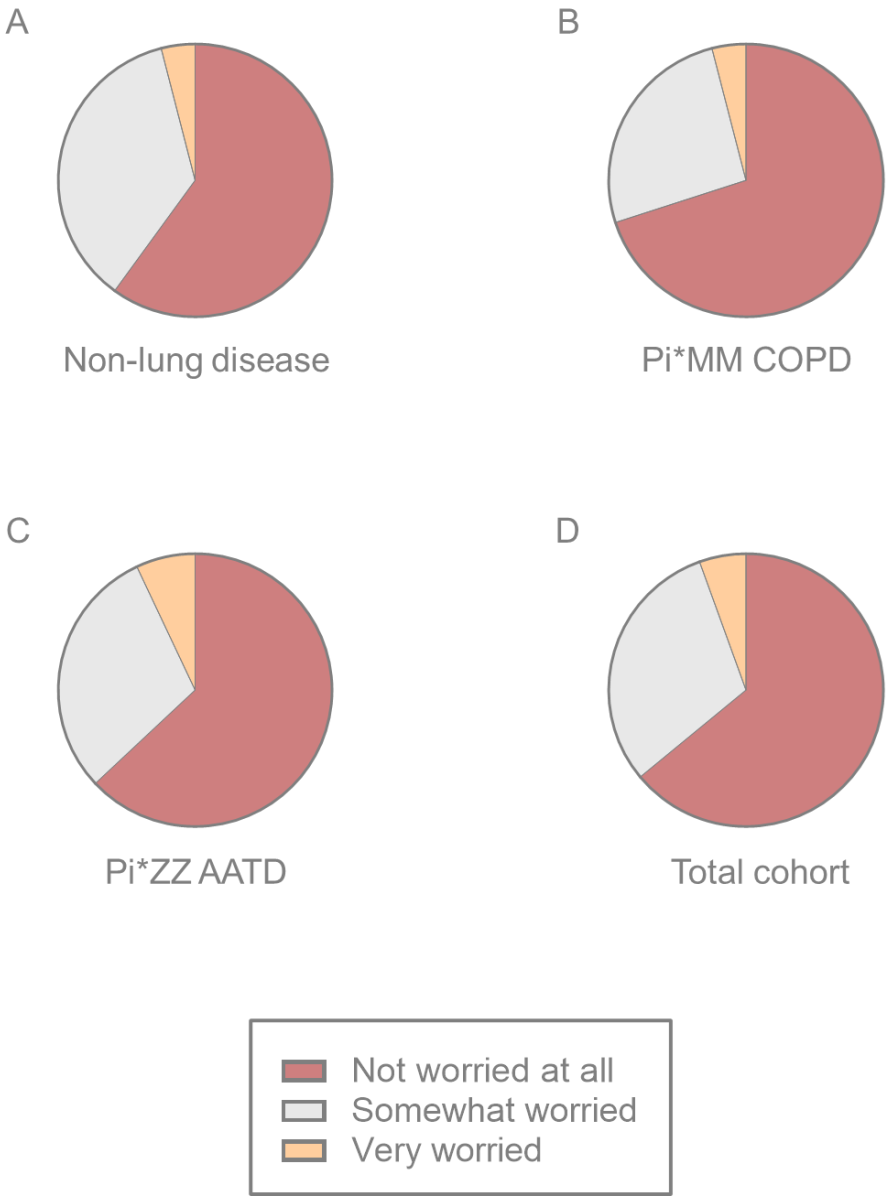

Figure S1. Study participant concerns regarding potential for severe adverse events prior to first ChAdOx1 nCoV-19 dose.
Patients with Pi*ZZ AATD (n=170) and Pi*MM COPD (n=150) and non-lung disease controls (n=140) were surveyed prior to receiving their first vaccination against COVID-19. Participants were asked to indicated the level of worry regarding potential severe adverse events against a three-level scale ("Not worried at all"/"Somewhat worried"/"Very worried"). Non-lung disease: "Not" = 84/140 (60.0%); "Somewhat" = 51/140 (36.4%); "Very" = 5/140 (3.6%). Pi*MM COPD: "Not" = 105/150 (70.0%); "Somewhat" = 39/150 (26.0%); "Very" = 6/150 (4.0%). Pi*ZZ AATD: "Not" = 108/170 (63.5%); "Somewhat" = 50/170 (29.4%); "Very" = 12/170 (7.1%). Total cohort: "Not" = 294/460 (63.9%); "Somewhat" = 138/460 (30.0%); "Very" = 26/460 (5.7%).

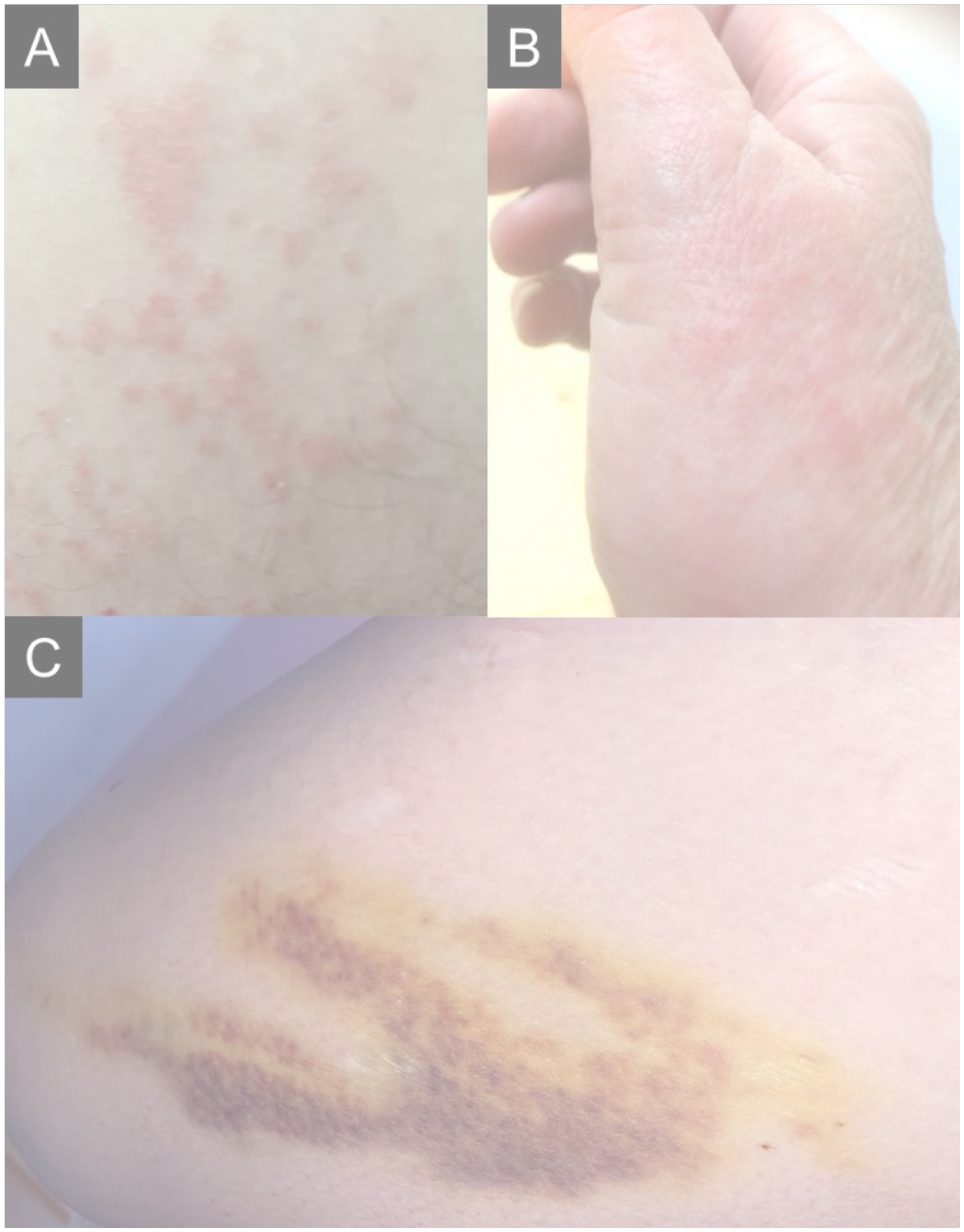

Figure S2. Post-vaccination cutaneous events in Pi*ZZ individuals.
Representative images of cutaneous adverse events in the study population. (A) Maculopapular rash. (B) Urticarial rash. (C) Unexplained bruising. Images reproduced with patient permission.