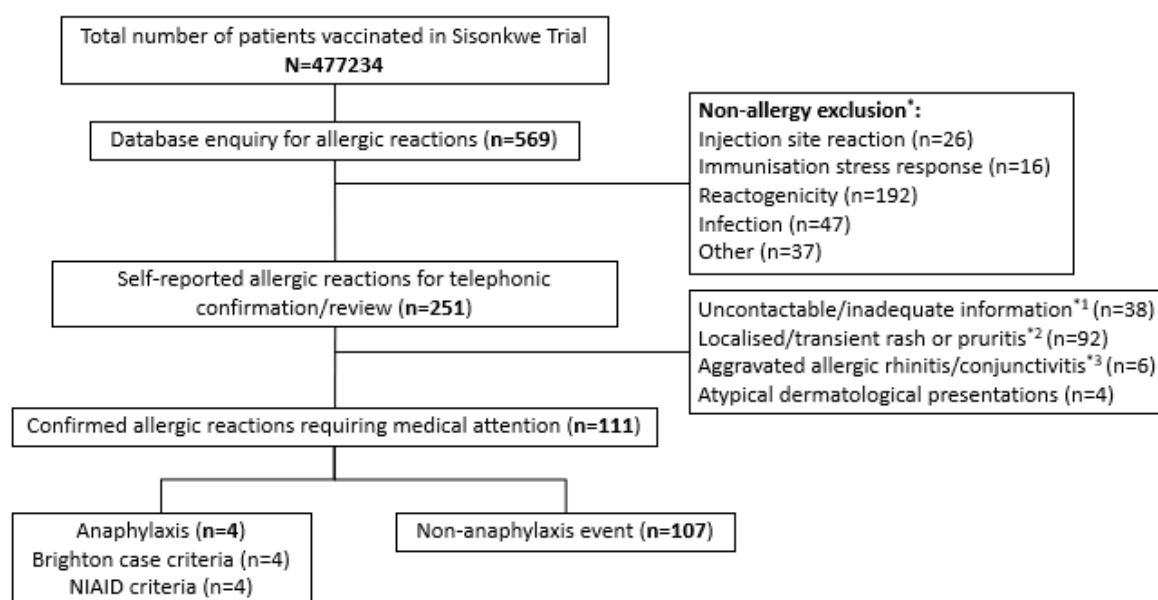


Figure 1. Overall summary of all allergy adverse events following immunisation with Janssen Ad26COV 2.S reported during the Sisonke phase 3B study



***Non-allergy exclusion definitions:**

Injection site reactions included swelling, redness and localized itching around the area of vaccination
Immunisation stress response included all symptoms related to anxiety including fainting and vasovagal episodes within a few minutes post vaccination

Reactogenicity included participants that reported one or more of: fever, rigors, muscle aches, nausea/vomiting, atypical chest pains, sore throat and/or cough within the first 72 hours post vaccination

Infections included: SARsCoV2 RT-PCR positivity, tonsillitis, upper and lower respiratory tract infection, and tooth abscess.

Other diagnoses included: uncontrolled hypertension, thromboembolism, neuralgia, trauma, shingles/HSV1 reactivation, uncontrolled hypertension, arthralgia and respiratory symptoms occurring >28 days post vaccination

***1Uncontactable or inadequate information** meant that despite three separate phone call attempts we were unable to get sufficient information about the adverse reaction to classify it as allergy or non-allergy

***2 Localised/transient rash or pruritis** needed to be a reported rash of any morphology that was self-limiting (lasting less than 24 hours), and responsive to over-the-counter medications with no requirement for any contact with either a family physician or emergency medical service

Suggest NIAID criteria written in full in legend for Fig 1 and Table 1

***3 Worsening of existing allergic rhinoconjunctivitis** Patients with previously diagnosed allergic rhinitis reported worsened symptoms after receiving the vaccine

Age	Sex	Time to reaction	General symptoms	Brighton score and allergy symptoms	NIAID score	Atopy history	Anaphylaxis history	Past Medical History	Previous COVID	Hospitalised	Adrenaline used	MC tryptase <6 hr post Rxn
52	F	10min	Nil	Level 1 Major: <ul style="list-style-type: none"> 1 Dermatological (angioedema) 1 Respiratory (bronchospasm) 1 Cardiovascular (Hypotension and loss of consciousness) 	Yes	Asthma Penicillin allergy	Yes (penicillin)	Systemic Lupus Fibromyalgia Hypothyroidism Anaemia	No	Yes	Yes	ND
56	F	10min	Headache	Level 1 Major: <ul style="list-style-type: none"> 1 Dermatological (angioedema) 1 Respiratory (bronchospasm) 	Yes	Asthma/Allergic rhinitis Eczema Sensitised to HDM, tree pollen Polysorbate 80 allergy	Yes (Yellow fever vaccine)	Hypertension Glaucoma	Yes	Yes	No	4.99µg/l (1.0-15.0)
35	F	6 hours	Fever	Level 1 Major: <ul style="list-style-type: none"> 1 Dermatological (generalised urticaria) 2 Cardiovascular (hypotension, tachycardia) 1 Respiratory (bronchospasm) 	Yes	Beta-lactam allergy, NSAID allergy	Yes (BLA, NSAID)	Nil	No	Yes	Yes	ND (Elevated IgE and CRP)
48	F	5min	Nil	Level 3 Minor <ul style="list-style-type: none"> Dermatological (generalised puritis without rash) Respiratory (non-productive cough, subjective dyspnoea, sensation of throat closure) 	Yes	Allergy to latex, sodium benzoate, local anaesthetic	Yes (local anaesthetic)	Nil	No	Emergency room only	Yes	ND

				<ul style="list-style-type: none"> GIT (nausea and vomiting) 									
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Table 1. Characteristics of four cases of adjudicated anaphylaxis meeting both Brighton collaboration and NIAID case definition

Abbreviations: GIT: gastrointestinal; NSAID: Nonsteroidal anti-inflammatory drug; BLA: Beta-lactam antibiotic; MC: mast cell; ND: Not done; NIAID: National Institute of Allergy and Infectious Disease

Table 2 Characteristics and management of non-anaphylaxis allergic AEFI stratified by timing of onset (immediate versus delayed)

	All cases, n=107	Immediate reaction ≤ 6 hours, n=24 [#]	All Delayed reaction > 6 hours, n=69 [#]	Isolated urticaria and/or angioedema n=70
Female, n(%)	91 (85)	21 (88)	57 (83)	60 (86)
Age, median(IQR) yrs.	38 (28;45)	38 (29; 52)	37 (27; 43)	39 (28; 46)
Time to reaction, median(IQR) hrs	24 (6;96)	0.75 (0.1; 3)	48 (22; 120)	48 (11.5; 120)
Allergy symptoms				
- Angioedema , n(%)	26 (24)	6 (25)	17 (25)	16 (27)
- Urticaria, n(%)	73 (68)	12 (50)	54 (78)	61 (87)
- Generalised pruritis, n(%)	30 (28)	7 (29)	22 (32)	18 (26)
- Respiratory symptoms ^{*1}	35(33)	12(50)	17(25)	excluded
- Gastrointestinal symptoms ^{*1}	11(10)	3(13)	5(7)	3 (4)
- Cardiovascular symptoms ^{*1}	7(7)	3 (13)	2(3)	excluded
Patients with reactogenic effects, n(%)	67 (63)	14 (58)	46 (67)	41 (56)
Local injection site reaction, n(%)	34 (32)	8 (33)	22 (32)	19 (27)
Allergy history				
None, n(%)	35 (33)	7 (29)	26 (38)	30 (43)
Unknown, n(%)	19 (18)	0	8 (12)	15 (21)
Any atopic disease, n (%)				
- previous any anaphylaxis, n(%)	6 (6) ^{*3}	3 (13)	3 (4)	3 (4)
- Drug allergy	11 (1)	4 (17)	7 (10)	5 (7)
- Asthma	26 (24)	9 (38)	16 (23)	8 (11)
- Atopic dermatitis	15 (14)	2 (8)	13 (12)	8 (11)
Past medical history				
- Unknown, n(%)	17 (15)	0	8 (12)	14 (20)
- None, n(%)	54 (50)	10 (42)	42 (60)	32 (45)
- HIV on ART, n(%)	3 (3)	1 (4)	2 (3)	3 (4)
- Patients with non communicable diseases	24 (22) ^{*4}	14 (58)	20 (29)	24 (34)
- COVID19 prior to vaccination, n(%)	6 (6)	4 (17)	2 (2)	4 (6)
Management				
Unknown, n(%)	14 (13)	0 (0)	5 (7)	13 (19)
Required treatment, n(%)	90 (84)	24 (100)	62 (90)	57 (81)
Hospitalised: Admitted, n(%)	8 (8)	3 (13)	5 (7)	1 (1)
Emergency Room visit, n(%)	11 (10)	4 (17)	7 (10)	4 (6)
Treatment(s) received				
- Adrenaline ^{*6} , n(%)	5 (5)	4 (17)	1 (1)	1 (1)
- Systemic Steroids, n(%)	30 (28)	12 (50)	18 (26)	11 (16)
- Antihistamines , n(%)	62 (58)	18 (75)	41 (59)	44 (63)
- Inhalational treatment, n(%) ^{*7}	36 (33)	9 (38)	10 (14)	0
- Other ^{*8}	16 (14)	3 (13)	13 (19)	13 (19)

#There were 14 participants in whom the time of reaction onset was unknown.

*¹ Respiratory symptoms included one or more of: bronchospasm, upper airway swelling, subjective dyspnoea without wheeze or stridor, persistent dry cough, hoarse voice, sensation of throat closure. Gastrointestinal symptoms included one or more of: nausea and vomiting, diarrhea, abdominal pain. Cardiovascular symptoms included one or more of hypotension, tachycardia, and decreased level of consciousness or loss of consciousness.

*² Reactogenicity adverse events include one or more of fever(n=49), headache(n=53), or myalgia(n=43)

*³ Anaphylaxis to latex (n=1), anaphylaxis to beta-lactam (n=1), anaphylaxis to bee venom (n=1), unknown (n=3) however no patients reported previous vaccine anaphylaxis

*⁴Non-communicable diseases include: HPT (n= 11), Diabetes (n=5), Dyslipidaemia (n=3), Hypothyroidism (n=5), GORD (n=3), PCOS (n=2), Gilberts disease (n=1), congenital heart disease (n=1), osteoporosis (n=2), breast cancer in remission (n=2), rheumatoid arthritis (n=1), endometriosis (n=1), osteoarthritis (n=1)

*⁶ Received adrenaline due to severe bronchospasm or angioedema of the face and tongue

*⁷ Nebulisation (n=12), inhaled corticosteroids (n=13), Long acting beta agonist/inhaled corticosteroid (n=2), Long acting beta agonist (n=2), Short acting beta agonist (n=1)

*⁸ Antibiotics (n=3), paracetamol (n=5), thiamine (n=1), intravenous fluids (n=6)

Supplementary Material

Appendix 1: Allergy search terms for safety database

1. "rash"
2. "hives"
3. "hive"
4. "urticaria"
5. "angioedema"
6. "angiedema"
7. "swollen tongue"
8. "allergic"
9. "allergy"
10. "pruritis"
11. "pruritus"
12. "itchiness"
13. "itchy"
14. "itchiness"
15. "itching"
16. "bronchospasm"
17. "bronchial"
18. "blocked chest"
19. "wheeze"
20. "wheezing"
21. "tightness chest"
22. "tight chest"
23. "difficulty breathing"
24. "shortness of breath"
25. "short of breath"
26. "sob"
27. "respiratory distress"
28. "dyspnoea"
29. "dyspnea"
30. "difficulty in breathing"
31. "difficulty breathing"
32. "diffculting breathing"
33. "diffcalty breathing"
34. "difficalty breathing"