EU RMP	
Drug Substance	Sipavibart
Version Number	2
Succession Number	3
Data lock point	29 April 2025
Date of final sign off	See e-signature page

EUROPEAN UNION RISK MANAGEMENT PLAN (EU RMP) for KAVIGALE ™ (sipavibart)

The content of this EU RMP has been reviewed and approved by the Marketing Authorisation Holder's QPPV or deputy QPPV, as delegated by the QPPV in the EU.

ADMINISTRATIVE INFORMATION

Rationale for update to RMP

Following European Medicines Agency (EMA) review, a recommendation was received that the safety concern of Cardiovascular and thromboembolic events (CVTEs) should not be included as an important potential risk but rather considered as a potential risk. Hence, this safety concern was removed from the EU Risk Management Plan (RMP).

Furthermore, the planned pregnancy PASS (D7000R00017), intended to assess the safety of sipavibart in pregnant women, is being withdrawn. The study is no longer feasible and will not be initiated due to limited patient exposure and the lack of activity of sipavibart against currently circulating variants. This decision is supported by the EMA Pharmacovigilance Risk Assessment Committee (PRAC), which recommended the removal of the PASS in its Type II Variation Assessment Report (EMA/VR/0000287106; dated 12 September 2025). AstraZeneca will continue to monitor the safety of sipavibart in pregnant women through routine pharmacovigilance activities.

Summary of significant changes in this RMP

Part 2 SV:	Included post-authorization exposure details
Part 2 SVII:	Removed Cardiovascular and thromboembolic events as a safety concern
Part 2 SVIII:	Removed Cardiovascular and thromboembolic events from the list of safety concerns
Part 3:	Removed the pregnancy PASS from the additional Pharmacovigilance activities.
Part 5	Removed the routine risk minimisation measures implemented for the safety topic: Cardiovascular and thromboembolic events Removed the pregnancy PASS from the additional Pharmacovigilance activities.
Part 6:	Removed Cardiovascular and thromboembolic events as important potential risk
Part 7: Annexes	Annex 4: Removed the Targeted Safety Questionnaires for Cardiovascular and thromboembolic events. Annex 8: Aligned to the updates throughout the RMP

Details of currently approved RMP

Version number	Version 1, Succession 2.0
Approved with procedure	EMEA/H/C/006291
Date of approval	24 February 2025

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation/ Special term	Definition/Explanation
ACE2	Angiotensin-converting enzyme 2
ADE	Antibody-dependent enhancement of disease
ATC	Anatomical Therapeutic Chemical [code]
CHO	Chinese hamster ovary
COVID-19	Coronavirus disease 2019
EEA	European Economic Area
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
F	Female
Fc	Fraction crystallisable
FcRn	Neonatal Fc receptor
GISAID	Global Initiative on Sharing All Influenza Data
GLP	Good Laboratory Practice
ICH	International Council for Harmonisation
ICU	Intensive Care Unit
IgG	Immunoglobulin G
IM	Intramuscular
INN	International Non-proprietary Name
IMP	Investigational medicinal product
IRR	Infusion-related reactions
ISR	Infusion-site reactions
IV	Intravenous
Little DIPPER	Study D7000C00004: A Phase I, Randomized, Safety and Pharmacokinetics Study of AZD3152 in Healthy Adults (Little DIPPER)
M	Male
mAb	Monoclonal antibody
N	Number of participants
NOAEL	No observed-adverse-effect-level
PASS	Post-authorisation safety study
PI	Prescribing information
PK	Pharmacokinetic
PrEP	Pre-Exposure Prophylaxis

Abbreviation/ Special term	**Definition/Explanation**
PSUR	Periodic Safety Update Report
Q	Quarter
RBD	Receptor binding domain
RMP	Risk Management Plan
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SmPC	Summary of product characteristics
SUPERNOVA	Study D7000C00001: Study Understanding Pre-Exposure pRophylaxis of NOVel Antibodies (SUPERNOVA)
TCR	Tissue cross reactivity
TM	L234F/L235E/P331S substitutions in the immunoglobulin heavy chain to reduce Fc receptor and C1q binding
UK	United Kingdom
US	United States
YTE	M252Y/S254T/T256E substitutions in the immunoglobulin heavy chain to increase FcRn affinity that results in the increased half-life of an antibody
WHO	World Health Organization

1 PART I: PRODUCT OVERVIEW

Table 1-1 Product Overview

Active substance(s) (INN or common name)	Sipavibart
Pharmacotherapeutic group(s) (ATC Code)	Immune sera and immunoglobulins, antiviral monoclonal antibodies (J06BD09)
Marketing Authorisation Applicant	AstraZeneca AB 15185 Södertälje, Sweden
Medicinal products to which this RMP refers	One
Invented name(s) in the European Economic Area (EEA)	KAVIGALE™
Marketing authorisation procedure	Centralised
Brief description of the product	Chemical class: Sipavibart is a monoclonal Immunoglobulin G1 (IgG1) antibody directed against the receptor binding domain (RBD) of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein.
	Summary of mode of action: Sipavibart binds to the receptor binding domain of the spike protein of the SARS-CoV-2 virus and blocks its interaction with the angiotensin-converting enzyme 2 (ACE2) host cellular receptor, blocking virus entry and effectively neutralising the SARS-CoV-2 virus.
	Important information about its composition: Sipavibart is a recombinant human immunoglobulin (Ig)G1 based antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. Sipavibart has been engineered with the YTE substitution to extend the monoclonal antibody half-life, and the TM substitution to reduce effector function, which is expected to reduce potential risk of antibody-dependent enhancement of infection or disease (ADE).
Hyperlink to the Product Information	KAVIGALE Summary of Product Characteristics (SmPC)
Indication(s) in the EEA	Sipavibart is indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents 12 years of age and older weighing at least 40 kg who are not currently infected with SARS- CoV-2 and who are immunocompromised due to a medical condition or receipt of immunosuppressive medications or treatments.
Dosage in the EEA	The recommended dose is 300 mg of sipavibart administered as an intramuscular (IM) injection or by a single intravenous (IV) infusion.
Pharmaceutical form(s) and strengths in the EEA.	Each carton contains one vial of 300 mg sipavibart in 2 mL (150 mg/mL). Clear to opalescent, and colourless to slightly yellow, pH 6.0 solution.

Table 1-1 Product Overview

Is/will the product be subject to additional monitoring in the EU?	Yes

2 PART II: SAFETY SPECIFICATION

2.1 MODULE SI: EPIDEMIOLOGY OF THE INDICATION(S) AND TARGET POPULATION

Incidence and prevalence:

COVID-19 is an infectious disease caused by SARS-CoV-2.

As of 07 October 2025, there had been over 778 million confirmed cases of COVID-19 worldwide, including approximately 7 million deaths, reported to the World Health Organization. In Europe, there have been over 281 million confirmed cases, including over 2.2 million deaths (WHO 2025).

COVID-19 variants

During the course of the pandemic, several SARS-CoV-2 variants with different patterns of infectivity have emerged (Hadj Hassine 2022, Joshi and Poduri 2022, Zhao et al 2022). Over time, the incidence of SARS-CoV-2 has varied widely and is mainly influenced by the dominant circulating variant and the vaccination status of the population at each given time. For example, a 2023 review of data across 50 countries reported a median incidence rate of 17.14 per 100,000 people during the Delta variant period and 61.66 per 100,000 people during the Omicron variant period (Wang et al 2023). AstraZeneca conducts continuous and thorough reviews of genomic databases such as Global Initiative on Sharing All Influenza Data (GISAID) for emerging variants. Demographics of the population in the proposed indication (age, gender, racial and ethnic origin) and risk factors for the disease:

Age

Individuals of any age can acquire SARS-CoV-2 infection, although the risk of severe COVID-19 increases with age, with those under the age of 18 years having a lower risk of acute COVID-19 infection, hospitalisation, or intensive care unit (ICU) admission compared to adults (CDC 2020, Livingston and Bucher 2020, ECDC 2023). In contrast, the risk for severe illness from COVID-19 increases with age, particularly in adults 70 years of age and older (Wu et al 2020, Chatterjee et al 2023).

Gender

The number of confirmed COVID-19 cases is comparable among men and women. Although men may have a slightly higher risk for more severe illness and higher mortality from

COVID-19 than women (Ramírez-Soto et al 2021), this is most likely due to a general difference in excess mortality rates between men and women (Nielsen et al 2021).

Racial and ethnic origin

Ethnicity (particularly non-White ethnicity) has been recognised as a predictor for more severe disease, and/or risk of hospitalisation in numerous studies (Gao et al 2021, Beaney et al 2022, Wang et al 2023). The main reasons for racial disparities in COVID-19 risk are socioeconomic status, contact with suspected or confirmed COVID-19 cases, and lack of access to clinical care (Lo et al 2021, Magesh et al 2021).

Immunocompromised population

The rollout of effective vaccines to protect against serious disease associated with COVID-19 has significantly reduced the morbidity and mortality associated with SARS-CoV-2 infection (Mohammad et al 2022). However, there still remains an unmet medical need for the approximately 2% to 3.9% of the immunocompromised population who remain at risk of severe and fatal COVID-19 due to their inability to mount an adequate response to complete active immunisation (Harpaz et al 2016, Lee et al 2022, Parker et al 2022, Evans et al 2023).

Compared to the general population, immunogenicity, the magnitude of immune response a vaccine generates over time, in the immunocompromised population is limited due to underlying disease or effect of immune suppressing therapy (Lee et al 2022). Immunocompromised patients, therefore, continue to be disproportionally affected by COVID-19. This group of patients often experiences poor clinical outcomes of COVID-19 such as severe disease, hospitalization, ICU admissions and deaths compared to immunocompetent individuals (Meeraus et al 2024, EMA 2024).

The main existing treatment options:

During the pandemic, at least 12 different COVID-19 vaccines have been administered globally (WHO 2022). Currently, 7 and 6 COVID-19 vaccines are authorized for use in the EU and UK, respectively, including originally authorized and adapted vaccines (EMA 2024, UK Health Security Agency 2024). As of March 2024, there are 3 approved COVID-19 vaccines for use in the USA (CDC 2024). These vaccines have significantly reduced the morbidity and mortality associated with SARS-CoV-2 infection (Mohammad et al 2022).

Vaccines, however, are not sufficient to protect the immunocompromised population who are unable to mount a protective immune response following vaccination. SARS-CoV-2 neutralizing mAbs such as EVUSHELD™ (tixagevimab and cilgavimab; AstraZeneca, EMEA/H/C/005788) provided vulnerable populations with much-needed protection, independent of immune system integrity.

Before SARS-CoV-2 variants in the BQ.1 lineage became dominant, SARS-CoV-2 neutralising monoclonal antibodies (mAbs) such as EVUSHELD (tixagevimab and cilgavimab; AstraZeneca, EMEA/H/C/005788) for pre-exposure prophylaxis (PrEP) provided vulnerable populations with much-needed protection, independent of immune system integrity. The emergence of BQ.1 variants significantly reduced the potency and neutralising activity of both components of EVUSHELD (Case et al 2022). EVUSHELD was withdrawn from the European market on 20 October 2025 due to lack of efficacy against the circulating variants. At this time, there are no authorised/approved COVID-19 PrEP mAbs in the EU that can effectively neutralise the currently circulating SARS-CoV-2 variants. Based on immunobridging data, Pemgarda™ (pemivibart injection, INVIVYD) is authorised for emergency use only in the US for COVID-19 PrEP for pre-exposure prophylaxis of COVID-19 in moderately to severely immunocompromised adolescents and adults. PEMGARDA is administered as a single 4500 mg intravenous infusion, with repeat dosing at the same dosage approximately every 3 months (FDA 2024).

Natural history of the indicated condition in the untreated population, including mortality and morbidity:

SARS-CoV-2 infection can be classified into asymptomatic, pre-symptomatic infection, mild, moderate, severe, and critical illness. Transmission of SARS-CoV-2 may occur from asymptomatic, pre-symptomatic or symptomatic individuals (Cascella et al 2021). Estimated rates of asymptomatic SARS-CoV-2 infection vary widely with an interquartile range of estimates across 130 studies ranging from 14% to 50% (prediction interval 2% to 90%) (Buitrago-Garcia et al 2022). Symptomatic patients can experience a range of symptoms from mild to critical illness, with shifts in patterns of reported symptoms relative to dominant variants throughout the pandemic (Schulze and Bayer 2022).

Recent research suggests a shift towards less severe clinical presentation of COVID-19 disease and a decrease in case fatality rates from 8.56 per 1000 persons during the Delta variant period to 3.04 per 1000 during the Omicron variant period; this is due to decreased pathogenicity of Omicron and increased vaccination coverage (Menni et al 2022, Greene et al 2023, Wang et al 2023, Zhao et al 2023). While there is a rapid increase in JN.1 infections, and likely increase in cases, the symptoms of JN.1 infection are similar and does not suggest that the associated disease severity is higher as compared to other circulating omicron variants.

Severe complications associated with COVID-19 include pneumonia, thromboembolism, circulatory shock, myocardial damage, arrhythmias, and encephalopathy (ECDC 2023).

2.2 MODULE SII: NON-CLINICAL PART OF THE SAFETY SPECIFICATION

Key safety findings from non-clinical studies and relevance to human usage:

- Development was initiated in 2022 for AZD5156, a combination of 2 monoclonal IgG1 antibodies, sipavibart (AZD3152) and cilgavimab (AZD1061), with broad neutralising activity across known SARS-CoV-2 variants. After careful evaluation of available in vitro neutralisation data, the landscape of circulating variants at the time, and recognition of Regulatory Agency feedback to consider continuing development of sipavibart alone, AstraZeneca decided to pursue sipavibart as a standalone therapy rather than in combination with cilgavimab. However, the non-clinical safety data generated with AZD5156 is applicable to sipavibart.
- The non-clinical programme for sipavibart consisted of studies conducted with AZD5156, as well as studies conducted with sipavibart alone. The programme included in vitro pharmacology studies that evaluated mAb binding kinetics, RBD epitope mapping, fraction crystallisable (Fc) receptor binding and effector function activity including antibody-dependent enhancement of infection, and SARS-CoV-2 neutralising antibody activity, as well as in vivo viral challenge studies conducted in hamsters. The programme also included one non-clinical pharmacokinetic (PK) study in human neonatal Fc receptor (FcRn) transgenic Tg32 mice, one repeat-dose IM and IV toxicology study in cynomolgus monkeys conducted with AZD5156, and 2 in vitro tissue cross reactivity (TCR) studies, conducted with AZD5156, and with each mAb component (sipavibart and cilgavimab).
- There were no safety issues identified in the non-clinical studies. Key findings from these studies are summarised below:
  - Sipavibart, an RBD-targeting mAb, potently neutralised SARS-CoV-2 variants not containing the F456L mutation, including contemporary variants BQ.1.1, XBB.1, XBB.1.5, and XBB.1.16. Sipavibart protected hamsters from SARS-CoV-2 disease and did not present any signs of antibody-dependent enhanced disease.
  - Similar PK was observed for sipavibart and cilgavimab in the cynomolgus monkeys following IM injection or IV infusion of 150 mg/kg of each mAb in the Good Laboratory Practice (GLP) toxicology study. Similar PK of sipavibart to cilgavimab was also observed in human FcRn transgenic mice following IV administration.
  - No binding to any tissues was observed in the TCR studies with sipavibart, confirming the absence of any potential off-target binding in adult or foetal human tissues.
  - Based on results from the repeat-dose toxicity study, sipavibart at 150 mg/kg, when dosed as a component of AZD5156 (300 mg/kg), was well tolerated in cynomolgus monkeys when administered once weekly for 3 weeks by IM injection or IV infusion. The no observed-adverse-effect-level (NOAEL) was considered to be 300 mg/kg AZD5156 (150 mg/kg for sipavibart) via IM or IV route of administration.

2.2.1 Toxicity

Key issues identified from acute or repeat-dose toxicity studies

No key findings identified.

Reproductive/developmental toxicity

In accordance with ICH S6 (R1), no studies were conducted, and no studies are planned to evaluate the effects of sipavibart on fertility or embryo-foetal and pre/postnatal development because sipavibart binds to a virus-specific target that is not expressed in non-clinical animal models or in humans. Further, sipavibart did not bind any of the evaluated adult human reproductive tissues (including placenta) nor any of the evaluated foetal human tissues in TCR studies.

Genotoxicity

No genotoxicity studies have been conducted with sipavibart. In accordance with ICH S6 (R1), genotoxicity testing has not been conducted, and is not planned, because it is not applicable to biotechnology-derived large protein products. Sipavibart, a mAb, is not expected to cross the nuclear or mitochondrial membranes to interact directly with DNA or other chromosomal materials.

Carcinogenicity

In accordance with ICH S6 (R1), carcinogenicity studies have not been conducted with sipavibart and are not planned given that the target for this product is a virus-specific target, which is not expressed in non-clinical animal models or in humans.

2.2.2 Safety Pharmacology

No dedicated safety pharmacology study has been conducted or is planned for sipavibart.

Cardiovascular safety pharmacology (electrocardiograms, heart rate, body temperature, and blood pressure), respiratory safety pharmacology (respiratory rate), and neurological safety pharmacology (neurological observational battery), were assessed as part of the repeat-dose toxicology study in cynomolgus monkeys. Sipavibart administered once weekly for 3 weeks by IM injection or IV infusion at 150 mg/kg as a component of AZD5156 (300 mg/kg) did not induce any changes in the safety pharmacology parameters assessed.

2.3 MODULE SIII: CLINICAL TRIAL EXPOSURE

A summary of exposure to sipavibart, based on data from the 3 completed studies as of a data cut-off date of 29-April-2025, is provided below. There is no change in exposure since the previous RMP data cut-off.

Safety assessment is primarily based on the final analysis of the completed Phase III SUPERNOVA Parent Study Main cohort (data cut-off date of 29 April 2025). Supportive safety analyses are derived from the completed Phase I and II studies (Little DIPPER and SUPERNOVA Sub-study) safety data post-dose (from SUPERNOVA Parent Study Sentinel Safety Cohort). Data were not pooled from these supportive studies due to differences in population (immunocompromised vs healthy participants, inclusion vs exclusion of adolescents 12 to <18 years), dose (300 mg to 1200 mg sipavibart, 600 mg AZD5156), and route of administration (IV vs IM). However, these study results are consistent, and demonstrate that sipavibart was well tolerated, regardless of route of administration, up to 600 mg IM and up to 1200 mg IV; there were no safety concerns or dose-limiting toxicities in these supportive studies.

At the data cut-off date for this RMP, a total of 2102 participants had been exposed to sipavibart. Exposure data are summarised by age group/gender and by race/ethnic origin for the SUPERNOVA Parent Study, Main Cohort, (Table 2-1 and Table 2-2), SUPERNOVA Parent Study, Sentinel Safety Cohort (Table 2-3 and Table 2-4), the SUPERNOVA Sub-study (Table 2-5 and Table 2-6) and Little DIPPER (Table 2-7 and Table 2-8).

Table 2-1 Age Group and Gender (SUPERNOVA Parent Study, Main Cohort)

	Participants	
Age group	**M**	**F**
Paediatrics (12 years to 17 years)	4	4
Adults (18 to 64 years)	439	616
Elderly (≥ 65 years)	272	334

The Main Cohort received sipavibart 300 mg IM given as 2 doses, 6 months apart.

The study population consisted of participants 12 years of age and older (weighing at least 40 kg) with conditions causing immune impairment.

Data lock: 29 March 2024 (Primary Analysis).

Table 2-2 Race and Ethnic Origin (SUPERNOVA Parent Study, Main Cohort)

Race/ethnic origin	**Participants**
Race	
American Indian or Alaskan Native	1
Asian	111
Black or African American	202
Native Hawaiian or Other Pacific Islander	5
White	1239
Other	22

Table 2-2 Race and Ethnic Origin (SUPERNOVA Parent Study, Main Cohort)

Race/ethnic origin	Participants
Multiple	42
Not reported	38
Missing	9
Total	1669
Ethnic origin	
Hispanic or Latino	354
Not Hispanic or Latino	1240
Not reported	75
Total	1669

The Main Cohort received sipavibart 300 mg IM given as 2 doses, 6 months apart.

The study population consisted of participants 12 years of age or older (weighing at least 40 kg) with conditions causing immune impairment.

Data lock: 29 March 2024 (Primary Analysis).

Table 2-3 Age Group and Gender (SUPERNOVA Parent Study, Sentinel Safety Cohort)

	Participants	
Age group	**M**	**F**
Adults (18-55 years)	18	23

At the data cut-off date for the RMP, data were available for the Sentinel Safety Cohort which received AZD5156 600 mg single dose (AZD1061 300 mg IM followed by sipavibart 300 mg IM).

The study population consisted of healthy volunteers.

Data lock: 10 November 2023 (Day 181 Interim Analysis).

Table 2-4 Race and Ethnic Origin (SUPERNOVA Parent Study, Sentinel Safety Cohort)

Race/ethnic origin	Participants
Race	
American Indian or Alaskan Native	0
Asian	1
Black or African American	11
Native Hawaiian or Other Pacific Islander	0
White	27
Other	2
Total	41

Table 2-4 Race and Ethnic Origin (SUPERNOVA Parent Study, Sentinel Safety Cohort)

Race/ethnic origin	Participants
Ethnic origin	
Hispanic or Latino	2
Not Hispanic or Latino	37
Not reported	2
Total	41

The Sentinel Safety Cohort received AZD5156 600 mg single dose (AZD1061 300 mg IM followed by sipavibart 300 mg IM).

The study population consisted of healthy volunteers.

Data lock: 10 November 2023 (Day 181 Interim Analysis).

Table 2-5 Age Group and Gender (SUPERNOVA Sub-study)

	Participants	
Age group	**M**	**F**
Adults (18-64 years)	119	132
Elderly (≥ 65 years)	23	38
Missing	0	0
Totals	142	170

Sipavibart 1200 mg IV single dose.

The study population consisted of participants who were immunocompromised (n = 18) or immunocompetent/healthy volunteers (n = 294).

Data lock: 10 November 2023 (Day 91 Interim Analysis).

Table 2-6 Race and Ethnic Origin (SUPERNOVA Sub-study)

Race/ethnic origin	Participants
Race	
American Indian or Alaskan Native	1
Asian	4
Black or African American	66
Native Hawaiian or Other Pacific Islander	2
White	234
Other	2
Multiple	2
Not reported	1
Total	312

Table 2-6 Race and Ethnic Origin (SUPERNOVA Sub-study)

Race/ethnic origin	Participants
Ethnic origin	
Hispanic or Latino	86
Not Hispanic or Latino	224
Not reported	2
Total	312

Sipavibart 1200 mg IV single dose.

The study population consisted of participants who were immunocompromised (n = 18) or healthy volunteers (n = 294).

Data lock: 10 November 2023 (Day 91 Interim Analysis).

Table 2-7 Age Group and Gender (Little DIPPER)

	Participants	
Age group	**M**	**F**
Adults (18-55 years)	45	35

Sipavibart 300 mg IM, 300 mg IV, 600 mg IM, 600 mg IV, or 1200 mg IV; single dose.

The study population consisted of healthy volunteers.

Data lock: 15 November 2023 (Day 91 Interim Analysis).

Table 2-8 Race and Ethnic Origin (Little DIPPER)

Race/ethnic origin	Participants
Race	
Asian	0
Black or African American	25
Native Hawaiian or Other Pacific Islander	0
White	53
Other	2
Multiple	0
Total	80
Ethnic origin	
Hispanic or Latino	7
Not Hispanic or Latino	73
Total	80

Sipavibart 300 mg IM, 300 mg IV, 600 mg IM, 600 mg IV, or 1200 mg IV; single dose.

The study population consisted of healthy volunteers.

Data lock: 15 November 2023 (Day 91 Interim Analysis).

2.4 MODULE SIV: POPULATIONS NOT STUDIED IN CLINICAL TRIALS

2.4.1 Exclusion Criteria in Pivotal Clinical Studies Within the Development Programme

Pregnancy

Reason for exclusion: Pregnant individuals are excluded from the clinical studies to avoid potential harm to the unborn foetus.

Is it considered to be included as missing information: Yes

Patients < 12 years of age

Reason for exclusion: This population was excluded from the clinical studies based on the general principle that patients younger than 12 years of age should not be exposed to an investigational medicinal product (IMP) where the benefit-risk profile for the intended adult population has not yet been established, rather than due to specific safety concerns.

Is it considered to be included as missing information: No

Rationale: The proposed indication for sipavibart is for patients aged 12 years and older weighing at least 40 kg; therefore, use in the population < 12 years of age is not anticipated and not relevant to include as missing information.

History of allergy to any component of the IMP or other mAbs

Reason for exclusion: Patients with known allergy/hypersensitivity to the active ingredient of sipavibart or excipients were excluded from the clinical studies because these individuals may have a higher risk of hypersensitivity (anaphylactic reaction).

Is it considered to be included as missing information: No

Rationale: Sipavibart will be contraindicated in patients with known hypersensitivity to the active substance or excipients; therefore, this population is not relevant for consideration as missing information.

Clinically significant bleeding disorder (eg, factor deficiency, coagulopathy, or platelet disorder), or prior history of significant bleeding or bruising following injections or venepuncture

Reason for exclusion: Patients with history of bleeding disorders were excluded from the clinical studies because they have an increased risk of injection haemorrhage or bruising following injection.

Is it considered to be included as missing information: No

Rationale: The safety profile for patients with significant bleeding disorders following injection is well understood. Prevention and management of injection site bleeding after injection is fully integrated into standard clinical practice. Use in this patient population does not require further characterisation. Therefore, this population/utilisation is not relevant for consideration as missing information.

Receipt of immunoglobulin or convalescent COVID-19 plasma 6 months prior to Visit 1, COVID-19 vaccine or COVID-19 infection within 3 months prior to Visit 1, or antiviral therapy for prophylaxis within at least 2 weeks prior to Visit 1

Reason for exclusion: To avoid factors that may confound the results to ensure interpretability of data.

Is it considered to be included as missing information: No

Rationale: This population was excluded to avoid factors that may confound interpretation of the results. There is no reason to suspect that the safety profile of sipavibart would be impacted by past COVID-19 infection, vaccination or medicines indicated for the prevention or treatment of SARS-CoV-2.

2.4.2 Limitations to Detect Adverse Reactions in Clinical Trial Development Programmes

The clinical development programme is unlikely to detect certain types of adverse reactions such as rare adverse reaction or adverse reactions with a long latency.

2.4.3 Limitations in Respect to Populations Typically Under-represented in Clinical Trial Development Programmes

Table 2-9 Exposure of Special Populations Included or Not in Clinical Trial Development Programmes

Type of special population	Exposure
Pregnant individuals	Not included in the clinical development programme.
Participants with relevant comorbidities:	
Participants with chronic liver disease	96
Participants with chronic kidney disease	496
Participants with cardiovascular disease	
• Coronary artery disease	215
• Cardiomyopathy	58
• Congestive heart failure	10

Table 2-9 Exposure of Special Populations Included or Not in Clinical Trial Development Programmes

Type of special population	Exposure
Participants who are immunocompromised	
• Taking immunosuppressive medications	1228
• Solid organ transplant	235
• Moderate or severe secondary immunodeficiencies	265
• Haematologic malignancy	272
Participants with relevant different ethnic origin:	
White	1239
Black or African American	2
Native Hawaiian or Other Pacific Islander	5
American Indian or Alaskan Native	1
Asian	111
Multiple	42
Hispanic or Latino	354
Subpopulations carrying relevant genetic polymorphisms	Not applicable

The table does not include any small number of participants who have been included in the studies outside any exclusion criteria.

Data derived from: SUPERNOVA Parent Study, Main Cohort (data lock: 29 March 2024, Primary Analysis) N=1669).

2.5 MODULE SV: POST-AUTHORISATION EXPERIENCE

2.5.1 Method used to calculate exposure

KAVIGALE (sipavibart) International Birth Date (IBD) is 27 December 2024; the post-marketing exposure data included in this section is based on the number of doses distributed of the commercial product. All doses of sipavibart are intended for the approved indication and route of administration.

Approximately, 4000 doses were distributed to approved countries, and all doses were distributed in the EU region. Based on the sales data as of 26 June 2025, 298 vials were sold in the EU region. However, information on number of doses administered by gender, ethnicity, and age category are not available.

There were no doses distributed to other countries where KAVIGALE (Sipavibart) was approved (Canada, Japan and Australia).

2.6 MODULE SVI: ADDITIONAL EU REQUIREMENTS FOR THE SAFETY SPECIFICATION

Potential for misuse for illegal purposes

No potential for misuse for illegal purposes is anticipated for sipavibart.

2.7 MODULE SVII: IDENTIFIED AND POTENTIAL RISKS

2.7.1 Identification of Safety Concerns in the Initial RMP Submission

The content of this section 2.7.1 presents the position at the time of the initial RMP (Version 1), it will not be updated.

2.7.1.1 Risk Not Considered Important for Inclusion in the List of Safety Concerns in the RMP

Reason for not including an identified or potential risk in the list of safety concerns in the initial (Version 1) EU RMP

Known potential risks that require no further characterisation as they are followed up via routine pharmacovigilance, namely through signal detection and adverse reaction reporting, and for which the risk minimisation messages in the product information are adhered to by prescribers (eg, actions being part of standard clinical practice in each EU Member State where the product is authorised):

- **Immediate (Type I) hypersensitivity reactions including anaphylaxis:** Immediate hypersensitivity including anaphylaxis, can range from non-serious reactions such as a rash, urticaria and pruritus to potentially acute serious allergic reaction with multi-organ-system involvement that can present as, or rapidly progress to, a severe life-threatening reaction requiring immediate medical attention. Acute allergic reactions may include hypotension, dyspnoea, cyanosis, respiratory failure, angioedema, hypotonia, and unresponsiveness (including shock). Monoclonal antibodies have the potential to cause anaphylaxis and other hypersensitivity reactions. Up to the data lock for the EU RMP Version 1 (29 March 2024), there were no related serious adverse events of anaphylaxis or serious hypersensitivity reactions reported in the participants exposed to sipavibart. Healthcare professionals are familiar with this risk, and the management of this risk is integrated into routine medical practice when administering protein-based infusion/injection therapies. Therefore, the risk of Immediate (Type I) hypersensitivity reactions including anaphylaxis is considered to be a potential risk not categorised as important for inclusion in the RMP. The potential risk of hypersensitivity, including anaphylaxis, will be followed up via routine pharmacovigilance namely through signal detection and adverse reaction reporting, and risk minimisation messages in the product information are expected to be adhered to by prescribers (see Section 4.3 and 4.4 of the SmPC).
- **Antibody-dependent enhancement of disease (ADE)**: ADE is a theoretical risk for all mAbs used for prevention of COVID-19. One of the syndromes of ADE involves

increased binding efficiency of virus-antibody complexes to Fc receptor bearing cells, which trigger virus entry. This mAb, sipavibart, has been designed with a modification to prevent binding to cellular Fc receptors, so the risk of ADE occurring via this mechanism should range from very low to none. Several non-clinical studies have been conducted to assess the potential risk of ADE following administration of sipavibart. The data are consistent with that from other mAbs with TM substitutions in their Fc region that reduce antibody effector function and support that sipavibart poses minimal theoretical risk for mediating ADE. Potential clinical outcomes resulting from ADE include lack of therapeutic effect progressing to unanticipated worsening of COVID-19, which has not been observed in the clinical trials to date. An impact on therapeutic effectiveness due to ADE is unlikely given the design of sipavibart. For these reasons, ADE is not considered to impact the benefit-risk profile of sipavibart.

Identified risks not considered important/known risks that do not impact the risk-benefit profile:

- **Infusion-related reactions (IRR) and Infusion/injection-site reactions (ISR)**: IRR and ISR are commonly observed following IV infusions/IM injections and have been reported in sipavibart clinical studies as common adverse drug reactions, which were generally mild or moderate in severity and self-limiting. Specific guidance on the administration of sipavibart for healthcare professionals is provided in the SmPC, and this is fully aligned with standard clinical practice for the management of IRRs following immunisation (see Section 4.4 and 4.8 of the SmPC).

2.7.1.2 Risks Considered Important for Inclusion in the List of Safety Concerns in the RMP

The following topics were classified as important risks in the initial (Version 1) EU RMP

Important identified risks

There are no important identified risks for sipavibart.

Important potential risks

There are no important potential risks for sipavibart.

Missing information: Use in pregnancy

Pregnant individuals are excluded from the clinical studies of sipavibart but are not contraindicated for sipavibart. Pregnant individuals are at an increased risk for severe illness from COVID-19 compared to nonpregnant individuals; therefore, further characterisation of use of sipavibart in pregnant individuals is needed.

Risk-benefit impact:

There are insufficient data to determine the safety profile in pregnant individuals. No binding to any tissues was observed in the TCR studies with sipavibart, confirming the absence of any potential off-target binding in adult or foetal human tissues. However, human Immunoglobulin G1 antibodies are known to cross the placental barrier; therefore, sipavibart has the potential to be transferred from the mother to the developing foetus. It is unknown whether the potential transfer of sipavibart provides any benefit or risk to the foetus (as per the SmPC, Section 4.6: "Sipavibart should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the foetus").

2.7.2 New Safety Concerns and Reclassification With a Submission of an Updated RMP

Following EMA's review (EMA/VR/0000287106; dated 12 September 2025), a recommendation was received that the safety concern of Cardiovascular and thromboembolic events (CVTEs) should not be included as an important potential risk but rather considered as a potential risk. Accordingly, this safety concern was removed from the EU RMP.

2.7.3 Details of Important Identified Risks, Important Potential Risks and Missing Information

2.7.3.1 Presentation of Important Identified Risks and Important Potential Risks

Important identified risks:

There are no important identified risks for sipavibart.

Important potential risks:

There are no important potential risks for sipavibart.

2.7.3.2 Presentation of Missing Information

Missing information: Use in pregnancy

Evidence source: One pregnancy report was received from the clinical trials in the sipavibart group. The participant delivered a healthy baby without any complications. Whilst non-clinical safety studies have not indicated any concerns, the effect of sipavibart on the foetus is unknown.

Population in need of further characterisation: The use of sipavibart during pregnancy was planned to be evaluated in a post-authorisation safety study (PASS). However, this PASS will not be initiated as the currently circulating variants are no longer susceptible to sipavibart resulting in minimal patient exposure. AstraZeneca will continue to monitor the safety of sipavibart in pregnant women through routine pharmacovigilance activities.

2.8 MODULE SVIII: SUMMARY OF THE SAFETY CONCERNS

2.8.1 Summary of the Safety Concerns

Table 2-10 Summary of Safety Concerns

Important identified risks	None
Important potential risks	None
Missing information	Use in pregnancy

3 PART III: PHARMACOVIGILANCE PLAN

3.1 ROUTINE PHARMACOVIGILANCE ACTIVITIES

AstraZeneca undertakes routine pharmacovigilance activities consistent with the ICH E2E Pharmacovigilance Planning Guideline. Routine pharmacovigilance activities (as defined by standard operating procedures and guidelines) are designed to rapidly assess the ongoing safety profile of sipavibart throughout clinical development and in the post-authorisation period in order to characterise and communicate pertinent safety data appropriately. A comprehensive description of all aspects of the pharmacovigilance system is provided in the Pharmacovigilance System Master File, which is available upon request.

Specific adverse reaction follow-up questionnaires for safety concerns:

There are no follow-up questionnaires for safety concerns for sipavibart.

Other forms of routine pharmacovigilance activities:

None

3.2 ADDITIONAL PHARMACOVIGILANCE ACTIVITIES

Not applicable.

3.3 SUMMARY TABLE OF ADDITIONAL PHARMACOVIGILANCE ACTIVITIES

Not applicable.

4 PART IV: PLANS FOR POST-AUTHORISATION EFFICACY STUDIES

This section is not applicable as no post-authorisation efficacy studies are planned.

5 PART V: RISK MINIMISATION MEASURES

5.1 ROUTINE RISK MINIMISATION MEASURES

Table 5-1 Description of Routine Risk Minimisation Measures by Safety Concern

Safety concern	Routine risk minimisation activities
Important identified risks	Not applicable
Important potential risks	Not applicable
Missing Information: Use in pregnancy	Routine risk communication: SmPC Section 4.6 and Package Leaflet. Routine risk minimisation activities recommending specific clinical measures to address the risk: None

5.2 ADDITIONAL RISK MINIMISATION MEASURES

Routine risk minimisation activities as described in Section 5.1 are sufficient to manage the safety concerns of the medicinal product.

5.3 SUMMARY OF RISK MINIMISATION MEASURES

Table 5-2 Summary Table of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Missing information: Use in pregnancy	Routine risk minimisation measures: SmPC Section 4.6 and Package Leaflet.	Not applicable

6 PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR KAVIGALE™ (SIPAVIBART)

This is a summary of the risk management plan (RMP) for KAVIGALE. The RMP details important risks of KAVIGALE how these risks can be minimised, and how more information will be obtained about the risks and uncertainties for KAVIGALE (missing information).

KAVIGALE's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how KAVIGALE should be used.

This summary of the RMP for KAVIGALE should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which are part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of KAVIGALE's RMP.

6.1 THE MEDICINE AND WHAT IT IS USED FOR

KAVIGALE is indicated for pre-exposure prophylaxis of COVID-19 in adults and adolescents 12 years of age and older weighing at least 40 kg who are not currently infected with SARS-CoV-2 and who are immunocompromised due to a medical condition or receipt of immunosuppressive medications or treatments.

It contains the monoclonal antibody KAVIGALE as the active substance and it is given by intramuscular (IM) injection *or* intravenous (IV) infusion.

Further information about the evaluation of KAVIGALE's benefits can be found in KAVIGALE's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

6.2 RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of KAVIGALE together with measures to minimise such risks and the proposed studies for learning more about KAVIGALE risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so as to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Reports (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of KAVIGALE is not yet available, it is listed under 'missing information' below.

6.2.1 List of Important Risks and Missing Information

Important risks of KAVIGALE are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of KAVIGALE. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine).

Table 6-1 List of Important Risks and Missing Information

Important identified risks	None
Important potential risks	None
Missing Information	Use in pregnancy

6.2.2 Summary of missing information

Table 6-2 Missing Information: Use in Pregnancy

Risk minimisation measures	Routine risk communication: SmPC Section 4.6, and Package Leaflet Routine risk minimisation activities recommending specific clinical measures to address the risk: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	None

6.2.3 Post-authorisation Development Plan

6.2.3.1 Studies Which are Conditions of the Marketing Authorisation

Not applicable.

6.2.3.2 Other Studies in Post-authorisation Development Plan

Not applicable.

7 PART VII: ANNEXES

ANNEX 4: SPECIFIC ADVERSE DRUG REACTION FOLLOW-UP FORMS (NOT APPLICABLE)

ANNEX 6: DETAILS OF PROPOSED ADDITIONAL RISK MINIMISATION ACTIVITIES (NOT APPLICABLE)

LIST OF REFERENCES

Beaney et al 2022
Beaney T, Neves AL, Alboksmaty A, Ashrafian H, Flott K, Fowler A, et al. Trends and associated factors for Covid-19 hospitalisation and fatality risk in 2.3 million adults in England. Nat Commun. 2022;13(1):2356.

Buitrago-Garcia et al 2022
Buitrago-Garcia D, Ipekci AM, Heron L, Imeri H, Araujo-Chaveron L, Arevalo-Rodriguez I, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: Update of a living systematic review and meta-analysis. PLoS Med. 2022;19(5):e1003987.

Cascella et al 2021
Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, evaluation, and treatment of Coronavirus (COVID-19). Updated 18 August 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan- [cited 4 September 2023]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/.

Case et al 2022
Case JB, Mackin S, Errico JM, Chong Z, Madden EA, Whitener B, et al. Resilience of S309 and AZD7442 monoclonal antibody treatments against infection by SARS-CoV-2 Omicron lineage strains. Nat Commun. 2022;13(1):3824.

CDC 2020
CDC Covid-19 Response Team. Coronavirus disease 2019 in children - United States, February 12 - April 2, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(14):422-6.

CDC 2024
CDC (Centers for Disease Control and Prevention). Stay Up to Date with COVID-19 Vaccines. [cited 2024 May 02]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html.

Chatterjee et al 2023
Chatterjee S, Nalla LV, Sharma M, Sharma N, Singh AA, Malim FM, et al. Association of COVID-19 with comorbidities: an update. ACS Pharmacol Transl Sci. 2023;6(3):334-54.

ECDC 2023
ECDC (European Centre for Disease Prevention and Control). 31 May 2023 [cited 2024 April 17]. https://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/covid-19/facts/clinical-features-and-sequelae.

EMA 2024
EMA (European Medicines Agency). COVID-19 medicines. [cited 2024 May 02]. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/public-health-threats/coronavirus-disease-covid-19/covid-19-medicines.

Evans et al 2023
Evans RA, Dube S, Lu Y, Yates M, Arnetorp S, Barnes E, et al. Impact of COVID-19 on immunocompromised populations during the Omicron era: insights from the observational population-based INFORM study. Lancet Reg Health Eur. 2023;35:100747.

FDA 2024
FDA (Food and Drug Administration). Fact Sheet for Patients, Parents, and Caregivers Emergency Use Authorization (EUA) of PEMGARDA (pemivibart) for Coronavirus Disease 2019 (COVID-19). [cited 2024 May 02]. Available from: https://www.fda.gov/media/177069/download.

Gao et al 2021
Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: A review. Allergy. 2021;76(2):428-55.

Greene et al 2023
Greene SK, Levin-Rector A, Kyaw NTT, Luoma E, Amin H, McGibbon E, et al. Comparative hospitalization risk for SARS-CoV-2 Omicron and Delta variant infections, by variant predominance periods and patient-level sequencing results, New York City, August 2021-January 2022. Influenza Other Respir Viruses. 2023;17(1):e13062.

Hadj Hassine 2022
Hadj Hassine I. Covid-19 vaccines and variants of concern: A review. Rev Med Virol. 2022;32(4):e2313.

Harpaz et al 2016
Harpaz R, Dahl RM, Dooling KL. Prevalence of Immunosuppression Among US Adults, 2013. JAMA. 2016;316(23):2547–8.

Joshi and Poduri 2022
Joshi G, Poduri R. Omicron, a new SARS-CoV-2 variant: assessing the impact on severity and vaccines efficacy. Hum Vaccin Immunother. 2022;18(1):2034458.

Lee et al 2022
Lee ARYB, Wong SY, Chai LYA, Lee SC, Lee MX, Muthiah MD, et al. Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis. BMJ. 2022;376:e068632.

Livingston and Bucher 2020
Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA. 2020;323(14):1335.

Lo et al 2021
Lo CH, Nguyen LH, Drew DA, Warner ET, Joshi AD, Graham MS, et al. Race, ethnicity, community-level socioeconomic factors, and risk of COVID-19 in the United States and the United Kingdom. EClinicalMedicine. 2021;38:101029.

Magesh et al 2021
Magesh S, John D, Li WT, Li Y, Mattingly-App A, Jain S, et al. Disparities in COVID-19 outcomes by race, ethnicity, and socioeconomic status: A systematic review and meta-analysis. JAMA Netw Open. 2021;4(11):e2134147.

Meeraus et al 2024
Meeraus W et al. High prevalence of immunocompromising conditions among patients with severe acute respiratory infection, including SARS-CoV-2: results from a multicentre, test-negative case-control study. Poster P0381. 34th ECCMID Global; 27 April 2024; Barcelona, Spain.

Menni et al 2022
Menni C, Valdes AM, Polidori L, Antonelli M, Penamakuri S, Nogal A, et al. Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of Omicron and Delta variant dominance: A prospective observational study from the ZOE COVID Study. Lancet 2022;399(10335):1618-24.

Mohammad et al 2022
Mohammed I, Nauman A, Paul P, Ganesan S, Chen KH, Jalil SMS, et al. The efficacy and effectiveness of the COVID-19 vaccines in reducing infection, severity, hospitalization, and mortality: a systematic review. Hum Vaccin Immunother. 2022;18(1):2027160.

Nielsen et al 2021
Nielsen J, Nørgaard SK, Lanzieri G, Vestergaard LS, Moelbak K. Sex-differences in COVID-19 associated excess mortality is not exceptional for the COVID-19 pandemic. Sci Rep. 2021;11(1):20815.

Parker et al 2022
Parker EK, Desai S, Marti M, Nohynek H, Kaslow DC, Kochhar S, et al. Response to additional Covid-19 vaccine doses in people who are immunocompromised: A rapid review. Lancet Glob Health. 2022;10(3):e326-8.

Ramírez-Soto et al 2021
Ramírez-Soto MC, Ortega-Cáceres G, Arroyo-Hernández H. Sex differences in COVID-19 fatality rate and risk of death: An analysis in 73 countries, 2020-2021. Infez Med. 2021;29(3):402-7.

Schulze and Bayer 2022
Schulze H and Bayer W. Changes in symptoms experienced by SARS-CoV-2-infected individuals – from the first wave to the Omicron variant. Front Virol. 2022;2:880707.

UK Health Security Agency 2024
UK Health Security Agency. COVID-19 vaccination programme. [cited 2024 May 02]. Available from: https://www.gov.uk/government/collections/covid-19-vaccination-programme.

Wang et al 2023
Wang C, Liu B, Zhang S, Huang N, Zhao T, Lu QB, et al. Differences in incidence and fatality of COVID-19 by SARS-CoV-2 Omicron variant versus Delta variant in relation to vaccine coverage: A world-wide review. J Med Virol. 2023;95(1):e28118.

WHO 2022
WHO (World Health Organization). 12 Vaccines Granted Emergency Use Listing (EUL). [cited 2024 May 02]. Available from: https://covid19.trackvaccines.org/agency/who/.

WHO 2025
WHO (World Health Organization). WHO COVID-19 dashboard. [cited 2025 October 26]. Available from: https://data.who.int/dashboards/covid19/.

Wu et al 2020
Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934-43.

Zhao et al 2022
Zhao S, Lou J, Cao L, Chong KC, Zee BCY, Chan PKS, et al. Differences in the case fatality risks associated with SARS-CoV-2 Delta and non-Delta variants in relation to vaccine coverage: An early ecological study in the United Kingdom. Infect Genet Evol. 2022;97:105162.

Zhao et al 2023
Zhao S, Luo K, Guo Y, Fang M, Sun Q, Dai Z, et al. Analysis of factors influencing the clinical severity of Omicron and Delta variants. Trop Med Infect Dis. 2023;8(6):330.

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