Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Australian Public Assessment Report for MVC COVID-19 Vaccine

Active ingredient: MVC-COV1901

Sponsor: Grand Pacific CRO Australia

September 2023

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Aged Care and is responsible for regulating therapeutic goods, including medicines, medical devices, and biologicals.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety, and efficacy.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to the Australian public outweigh any risks associated with the use of therapeutic goods.
- The TGA relies on the public, healthcare professionals and industry to report problems with therapeutic goods. The TGA investigates reports received to determine any necessary regulatory action.
- To report a problem with a therapeutic good, please see the information on the TGA website.

About AusPARs

- The Australian Public Assessment Report (AusPAR) provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve a prescription medicine submission. Further information can be found in Australian Public Assessment Report (AusPAR) guidance.
- AusPARs are prepared and published by the TGA.
- AusPARs are static documents that provide information that relates to a submission at a particular point in time. The publication of an AusPAR is an important part of the transparency of the TGA's decision-making process.
- A new AusPAR may be provided to reflect changes to indications or major variations to a prescription medicine subject to evaluation by the TGA.

Contents

List of abbreviations

Abbreviation	Meaning
ACV	Advisory Committee on Vaccines
ARTG	Australian Register of Therapeutic Goods
ASA	Australia specific annex
CMI	Consumer Medicines Information
DLP	Data lock point
EU	European Union
GMT	Geometric mean titre
IgG	Immunoglobin G
MVC	MVC COVID-19 vaccine
nAb	Neutralising antibody
PI	Product Information
PSUR	Periodic safety update report
RAT	Rapid antigen test
RMP	Risk management plan
SAR-CoV-2	Severe acute respiratory syndrome coronavirus 2
S-P2	Spike protein
TGA	Therapeutic Goods Administration
VE	Vaccine efficacy

Product submission

Submission details

Type of submission:	New biological entity
Product name:	MVC COVID-19 Vaccine
Active ingredient:	MVC-COV1901
Decision:	Withdrawn
Date of decision:	Not applicable
Date of entry on ARTG	Not applicable
ARTG numbers	Not applicable
▼ *Black Triangle Scheme*	Not applicable
Sponsor's name and address:	Grand Pacific CRO Australia Suite 201, Level 2 1 - 9 Chandos Street, NSW 2065
Dose form:	Suspension for injection
Strength:	15 µg/0.5 mL
Containers:	Multi-dose vial (10 doses per vial) and pre-filled syringe
Pack size:	Not applicable
Approved therapeutic use for the current submission:	Not applicable
Route of administration:	Intramuscular injection
Dosage:	Not applicable
Pregnancy category:	B2 Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage. The use of any medicine during pregnancy requires careful consideration of both risks and benefits by the treating health professional. This must not be used as the sole basis of decision making in the use of medicines during pregnancy. The TGA does not provide advice on the use of medicines in pregnancy for specific cases. More information is available from obstetric drug information services in your State or Territory.

Product background

This AusPAR describes the submission by Grand Pacific Cro Australia (the sponsor) to register MVC COVID-19 Vaccine (MVC-COV1901) 15 µg/0.5 mL, suspension for injection, vial and pre-filled syringe for the following proposed indication:[1]

> *For active immunisation to prevent novel coronavirus disease (COVID-19, also known as severe pneumonia with novel pathogens) in individuals 12 years of age and older. The decision to approve this indication has been made on the basis of safety, immunogenicity, and efficacy data in completed and ongoing clinical trials and immunobridging studies. Continued approval of this indication depends on verification and description of benefit in confirmatory trials and post-market assessment.*
>
> *This vaccine should be administered in accordance with the COVID-19 vaccination plan of the Central Epidemic Command Centre.*

This submission seeks the provisional registration of MVC COVID-19 Vaccine (MVC), a new vaccine providing immunisation against coronavirus-19 disease (COVID-19).

The MVC COVID-19 vaccine is a protein subunit vaccine consisting recombinant form of the SARS-CoV-2 spike (S) protein. This is adjuvanted with CpG 1018 (cystosine phosphoguanine 1018) and aluminium hydroxide, acting as adjuvants which enhance recognition by the innate immune system.

The proposed new vaccine is to be supplied in the form of two presentations, a multi-dose vial containing 10 doses per vial and a single-use, single-patient pre-filled syringe.

For both presentations, each dose of MVC COVID-19 vaccine (0.5 mL) contains 15 µg SARS-CoV-2 rS (MVC-COV1901).

A two-dose primary vaccination series is proposed, consisting of 15 µg at Days 0 and 28 given via intramuscular injection.

In support of this submission, the sponsor submitted a number of Phase II and Phase III studies, with the Phase III studies using the Vaxzevria COVID-19 vaccine as comparator.[2],[3] Vaxzevria COVID-19 vaccine (formerly known as AstraZeneca COVID-19 vaccine) was first approved in Australia (via provisional registration) on 15 February 2021. Unlike the MVC COVID-19 vaccine, which is a protein subunit vaccine, Vaxzevria is a viral vector vaccine. Vaxzevria is an adjuvated vaccine containing ChAdOx1 as its active ingredient.

The sponsor also provided additional information in response to the TGA first round evaluations questions, including Real World data from the Taiwan Food and Drug Administration regarding vaccine efficacy and utilisation in Taiwan during the pandemic.

Regulatory status

This product is considered a new chemical entity medicine for Australian regulatory purposes.

[1] This is the original indication proposed by the sponsor when the TGA commenced the evaluation of this submission. It may differ to the final indication approved by the TGA and registered on the Australian Register of Therapeutic Goods.

[2] Vaxzevria COVID-19 vaccine (formerly AstraZeneca COVID-19 vaccine) 1 x 1011 viral particles (vp; ChAdOx1)/mL, solution for injection. ARTG number: 349072.

[3] Vaxzevria AusPAR available at https://www.tga.gov.au/resources/auspar/auspar-chadox1-s

At the time the TGA considered this submission, a similar submission had been granted Emergency Use Authorisation in Taiwan on 15 June 2021, in Paraguay on 12 August 2021 and The Kingdom of Eswatini on 12 October 2021.

The following table summarises these submissions and provides the indications where approved.

Table 1: International regulatory status

Region	Status	Approved indications
Taiwan	Emergency Use Authorisation granted on 15 June 2021	*MVC COVID-19 vaccine is indicated for active immunisation to prevent novel coronavirus disease (COVID-19, also known as severe pneumonia with novel pathogens) in individuals 20 years of age and older.*
Paraguay	Emergency Use Authorisation granted on 12 August 2021	*MVC COVID-19 vaccine is indicated for active immunisation to prevent novel coronavirus disease (COVID-19, also known as severe pneumonia with novel pathogens) in individuals 18 years of age and older.*
The Kingdom of Eswantini	Emergency Use Authorisation granted on 12 October 2021	*MVC COVID-19 vaccine is indicated for active immunisation to prevent novel coronavirus disease (COVID-19, also known as severe pneumonia with novel pathogens) in individuals 20 years of age and older.*

Registration timeline

The following table captures the key steps and dates for this submission.

Data were provided as a rolling submission. Under normal circumstances, TGA's assessment (for both provisional and general registration) begins once all information to support registration is available. As part of the Department of Health and Aged Care's response to the pandemic, the TGA has agreed to accept rolling data for COVID-19 vaccines and treatments, to enable early evaluation of data as it becomes available.

Description	Date
Determination (Provisional) Extension	16 November 2022 2 May 2022
Submission dossier accepted	7 June 2022
Evaluation completed	24 May 2023
Delegate's Overall benefit-risk assessment and request for Advisory Committee advice	25 May 2023
Sponsor's pre-Advisory Committee response	30 May 2023

Description	Date
Advisory Committee meeting	7 June 2023
Registration decision (Withdrawal)	25 July 2023

Submission overview and risk/benefit assessment

A summary of the TGA's assessment for this submission is provided below.

Quality

The MVC COVID-19 Vaccine (MVC-COV1901) is a protein subunit vaccine based on the stable prefusion spike protein (S-2P) with adjuvants.

The MVC COVID-19 Vaccine contains recombinant SARS-CoV-2 spike protein (SARS-CoV-2 rS), known as MVC-COV1901, produced using recombinant Chinese hamster ovary cell line transfected with a plasmid containing the gene sequence for S-P2. The vaccine formulation contains aluminium hydroxide and CpG1018 oligonucleotide adjuvants and is formulated with phosphate buffered saline.

The proposed vaccine is available in two container presentations, as follows:

- MVC COVID-19 Vaccine 15 µg/0.5 mL injection suspension pre-filled syringe
- MVC COVID-19 Vaccine 15 µg /0.5 mL injection suspension multi-dose vial (10 x 0.5 mL doses).

There are significant issues identified from the TGA's quality evaluation of the submitted data that would indicate the product should not be provisionally registered on the basis of quality, or safety-related issues arising from the quality of the product. The manufacturing quality information submitted by the sponsor has outstanding issues that need to be addressed before a recommendation can be made regarding the provisional registration of MVC COVID-19 Vaccine from a quality and pharmaceutical chemistry perspective.

Nonclinical

The sponsor has conducted adequate studies on pharmacology and toxicity of the vaccine, except that the potential effects of the novel adjuvant (CpG1018) on embryofetal development were not fully studied.

The composition of the nonclinical dossier submitted met regulatory guidelines for vaccines and the toxicity studies were conducted in compliance with Good Laboratory Practices. The nonclinical studies with adjuvant CpG 1018 were submitted to the TGA by Dynavax Technologies, the company responsible for development and commercialisation of adjuvant CpG 1018. These studies were assessed separately during the TGA's nonclinical evaluation.

The MVC-COV1901 vaccine was shown to be immunogenic in mice, rats and hamsters and induced both humoral (virus neutralising antibodies) and cellular immune (T-helper 1 cell biased) response in mice, rats and hamsters. However, the immunoglobin G (IgG) and

neutralising antibodies (nAb) declined on Day 57 (four weeks after the third injection) in the rat repeat-dose toxicity study.

The vaccine provided some protection from infection in hamsters when challenged four weeks after the second vaccine dose based on viral RNA load and lung pathology. The vaccine dose in hamsters (10 μg/kg or 50 μg/kg) was higher than the proposed clinical human dose of 15 μg (0.3 μg/kg). There were no protection studies in non-human primates, no long-term immunity data and no data on immunity against variants in animal models.

The novel CpG 1018 adjuvant is a toll-like receptor 9 (TLR9) agonist and was shown to simulate TLR9-mediated immunostimulatory activity. Pre-fusion-stabilised spike protein (S-2P) adjuvanted with both CpG 1018 and aluminium hydroxide elicited higher nAb titres than S-2P adjuvanted with a single adjuvant (either CpG 1018 or aluminium hydroxide alone) in mice.

Examination of safety pharmacology (incorporated into general toxicity studies) revealed no effects of MVC-COV1901 on central nervous system or respiratory function in rats. Effects on cardiovascular function were not studied for the vaccine, but the adjuvant CpG1018 did not alter cardiovascular function in animal species. Noting myocarditis and pericarditis are noted as potential risks of the MVC-COV1901 vaccine in the risk management plan (RMP), the effect of MVC-COV1901 vaccine on cardiovascular function needs to be addressed by clinical data.

There are no pharmacokinetic data on the MVC-COV1901 vaccine, consistent with the relevant guidelines. Limited studies in rats and monkeys with the adjuvant CpG 1018 showed low plasma concentrations and rapid clearance after relatively high subcutaneous doses (up to 12.5 mg/kg), consistent with literature data for other CpG oligodeoxynucleotides. As per literature data and findings from the toxicity studies, adjuvant CpG 1018 is expected to be distributed to kidney, liver, spleen, bone marrow and lymph nodes.

The repeat-dose studies in rats were adequately conducted, achieving high relative exposures (at least about 667 times and 400 times the clinical dose on a μg/kg basis for the S-2P and adjuvant CpG 1018, respectively). The MVC-COV1901 vaccine was well tolerated in rats without evidence of systemic toxicity. The anticipated pharmacological responses (injection site reactions characterised by swelling, granulomatous inflammation, multifocal slight mineralisation/necrosis, increased cellular infiltration and minimal to moderate oedema/erythema, clinical pathology, and tissue pathology) were consistent with immune stimulation and inflammation responses mostly attributed to adjuvant class effects. Kupffer cell hypertrophy in liver and lymphoid hyperplasia, plasmacytosis and/or heterophil infiltrates in draining lymph nodes, thymus, and spleen were observed in rats treated with adjuvant CpG1018 with or without S-2P. All effects were either partially or fully reversible after 4 weeks of recovery.

There is a theoretic risk of increased autoimmunity due to immunostimulation induced by CpG1018. Limited nonclinical data did not indicate induction of autoimmunity, However, considering the limitations of animal models to predict the risk of autoimmunity in humans, the potential for induction of autoimmunity or enhancement of autoimmune diseases should be assessed by clinical data.

Based on the dosing regimen and infrequent use in humans, MVC-COV1901 vaccine is not expected to be genotoxic or carcinogenic. CpG1018 was not genotoxic in a standard battery of genotoxicity tests.

In rats, administration of the MVC-COV1901 vaccine by intramuscular injection using adequate antigen doses (5 μg or 25 μg /dose, up to 200 times the human dose per kg body weight) did not raise safety concerns regarding female fertility, embryofetal development or postnatal development of offspring in a combined reproductive and developmental toxicity study.

However, embryofetal toxicity was reported for other CpG oligodeoxynucleotides in published studies. Noting the novelty of CpG adjuvants, embryofetal toxicity in animals reported for other CpG adjuvants and the absence of evaluation of potential effects of adjuvant CpG 1018 treatment during the full organogenesis period, it is recommended the vaccine not be used in pregnant women. Maternal antibodies were transferred across the placenta and/or through milk to the offspring, respectively, in rats.

The nonclinical evaluator has noted that there was no nonclinical evaluation of cardiovascular toxicity, which may be relevant to the incidence of myocarditis. They have also not recommended the vaccine for use in pregnant women. The nonclinical evaluator has recommended pregnancy class B2.[4]

Clinical

The clinical dossier included three Phase III studies which have compared immunogenicity endpoints in subjects receiving the MVC COVID-19 vaccine with those receiving Vaxzevria. Vaxzevria COVID-19 vaccine (formerly known as AstraZeneca COVID-19 vaccine) was first approved in Australia (via provisional registration) on 15 February 2021.[5] Unlike the MVC COVID-19 vaccine, which is a protein subunit vaccine, Vaxzevria is a viral vector vaccine. Vaxzevria is an adjuvated vaccine containing ChAdOx1 as its active ingredient.

These studies are:

- Study CT-COV-31, primary immunogenicity endpoint measured 14 days after second dose
- Study CT-COV-32, primary immunogenicity endpoint measured 14 days after second dose
- Study CT-COV-34, primary immunogenicity endpoint measured 14 days after second dose.

The clinical dossier also contained other, non-comparator studies including:

- Study CT-COV-22, a Phase II study, examined immunogenicity in adolescents, endpoints measured 28 days after second dose.
- Study CT-COV-21, a large Phase II study, examined immunogenicity in adults
- Study CT-COV-11 was a small Phase I study that examined similar immunogenicity endpoints to the Phase III studies.

The sponsor also provided additional information in response to the TGA first round evaluations questions, including Real World data from the Taiwan Food and Drug Administration regarding vaccine efficacy and utilisation in Taiwan during the pandemic.

Pharmacology

Pharmacokinetics

As this is a locally administered vaccine, pharmacokinetic data was not submitted.

[4] Category B2: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

[5] Vaxzevria COVID-19 vaccine (formerly AstraZeneca COVID-19 vaccine) 1 x 1011 viral particles (vp; ChAdOx1)/mL, solution for injection. ARTG number: 349072.

Pharmacodynamics

The main pharmacodynamic endpoint examined was the induction of neutralising antibodies. This was also assessed as an efficacy endpoint in the efficacy studies submitted.

Study CT-COV-11

Study CT-COV-11 examined the immune response to the MVC COVID-19 Vaccine in healthy subjects allocated to three arms with 15 participants in each arm. All participants received a two-dose schedule of MVC COVID-19 Vaccine. The three arms were based on doses of 5 µg followed by 5 µg; 15 µg followed by 15 µg; or 25 µg followed by 25 µg, with 28 days between the first and second doses.

At 28 days after the second dose (study Visit 8/Day 57), the mean geometric mean titre (GMT) for wild type SARS-CoV-2 neutralisation had increased 9.2-, 13.1- and 20.5-fold from Baseline in the low, mid and high dose arms respectively (Table 2).

Table 2: Study CT-COV-11 SARS-CoV2 wild type neutralisation geometric mean titre

Wild Type				
Geometric Mean Titer by Visit	**5 mcg**	**15 mcg**	**25 mcg**	**Total**
Visit 2 (Baseline)				
N (Missing)	15 (0)	15 (0)	15 (0)	45 (0)
GMT (t) (95% CI)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 4.0000)
Group Diff *p*-value (t)	*p* = NA (5 mcg – 15 mcg)			
	p = NA (5 mcg – 25 mcg)			
	p = NA (15 mcg – 25 mcg)			
Visit 4 (Day 15)				
N (Missing)	15 (0)	15 (0)	15 (0)	45 (0)
GMT (w) (95% CI)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 4.0000)
Group Diff *p*-value (w)	*p* = 0.1750 (5 mcg – 15 mcg)			
	p = 0.0902 (5 mcg – 25 mcg)			
	p = 0.7040 (15 mcg – 25 mcg)			
Visit 5 (Day 29)				
N (Missing)	15 (0)	15 (0)	15 (0)	45 (0)
GMT (w) (95% CI)	4.000 (4.0000, 4.0000)	4.000 (4.0000, 22.3900)	8.000 (4.0000, 8.0000)	4.000 (4.0000, 4.0000)
Group Diff *p*-value (w)	*p* = 0.0250* (5 mcg – 15 mcg)			
	p = 0.0033* (5 mcg – 25 mcg)			
	p = 0.6794 (15 mcg – 25 mcg)			
Visit 7 (Day 43)				
N (Missing)	15 (0)	15 (0)	15 (0)	45 (0)
GMT (t) (95% CI)	33.317 (18.5239, 59.9256)	76.307 (53.7497, 108.3309)	167.402 (122.0492, 229.6090)	75.220 (55.4283, 102.0784)
Group Diff (t) *p*-value	*p* = 0.0147* (5 mcg – 15 mcg)			
	p = <0.0001* (5 mcg – 25 mcg)			
	p = 0.0013* (15 mcg – 25 mcg)			

This corresponded to a seroconversion rate (an increase of greater than 4 times baseline GMT) of 80%, 100% and 100% for the low, mid and high dose arms respectively. The endpoints were measured against wild type COVID virus antigen.

Study CT-COV-25

Study CT-COV-25 examined the immune response in healthy subjects using a B.1.351 (Beta strain) of COVID. The Delegate noted that this study used significantly different dosing schedules than proposed in this submission.

Efficacy

Study CT-COV-31

Study CT-COV-31 was a Phase III study designed to assess the immunogenicity and safety of the MVC COVID-19 Vaccine compared with the Vaxzervria COVID-19 vaccine in adult volunteers. The MVC COVID-19 arm (n = 520) and Vaxzervria (n = 510) arms received a two-dose schedule administered at Day 0 and 28.

The primary endpoints were:

- Geometric mean titre of neutralising antibodies at 14 days after the second dose (Day 43) measured on the first 225 evaluable patients. The objective was to demonstrate the superiority of the MVC COVID-19 vaccine to the Vaxzervria vaccine.
- Seroconversion (4 fold increase in neutralising antibody titre) at 14 days post second dose. The objective was to demonstrate non-inferiority of the MVC COVID-19 Vaccine to the Vaxzervria vaccine.

Included patients were almost entirely seronegative against wildtype COVID at enrolment (95.9%), but about half (57.5%) had positive anti-N antibody tests on rapid antigen test (RAT) prior to vaccination.

The study population had a mean age of 32.1 years and was predominantly male (60.1%) (Figure 1).

Figure 1: Study CT-COV-31 Patient disposition

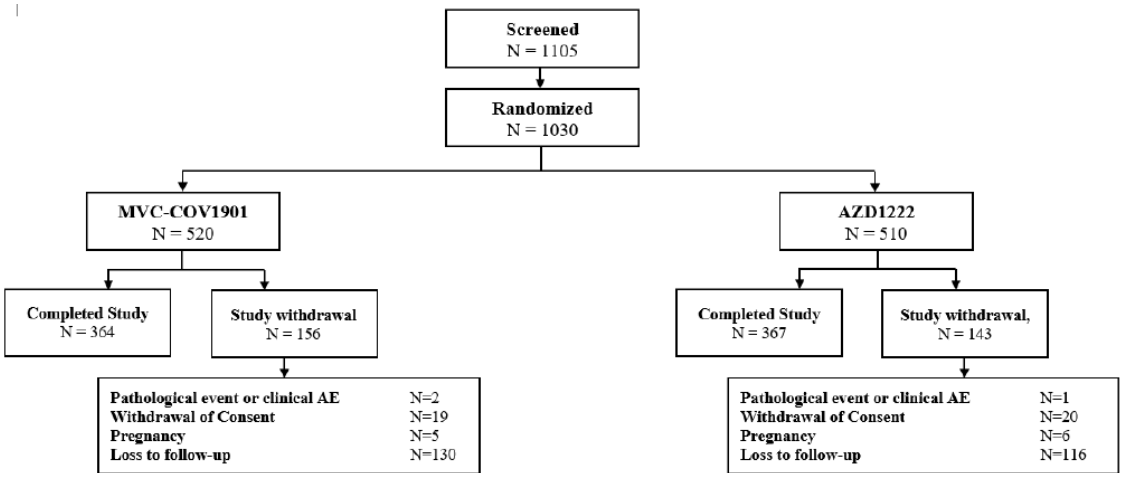


Table 3: Study CT-COV-31 Geometric mean titres and geometric mean titre ratio of the neutralising antibody (wild type) at Visit 4/Day 43 (per protocol immunogenicity analysis set)

Visit	Statistics	MVC-COV1901	AZD-1222	GMTR (MVC/AZ) [1]	*p*-value [2]
All Participants in the PPI Analysis Set, N		**116**	**109**		
Day 1 (Prior to 1st dose)	n	116	109	2.4 (95% CI: 1.6-3.4)	
	GMT	26.5	28.9		0.79
	95% CI of GMT	(20.0-35.2)	(21.6-38.7)		
Day 43 (14 days after 2nd dose)	n	116	109		
	GMT	1087.8	461.3		<0.001
	95% CI of GMT	(896.8-1319.5)	(338.0-629.5)		
	n	116	109		
	GMT Ratio	41	16		<0.001
	95% CI of GMT Ratio	(33.3-50.5)	(12.6-20.3)		
Subgroup: Seronaive in the PPI Analysis Set		**44**	**39**		
Day 1 (Prior to 1st dose)	n	44	39	4.9 (95% CI: 3.1-7.8)	
	GMT	5.04	5.04		-
	95% CI of GMT	(5.04-5.04)	(5.04-5.04)		
Day 43 (14 days after 2nd dose)	n	44	39		
	GMT	434.6	90.4		<0.001
	95% CI of GMT	(333.4-566.5)	(61.1-133.9)		
	n	44	39		
	GMT Ratio	86.2	17.9		<0.001
	95% CI of GMT ratio	(66.1-112.4)	(12.1-26.6)		

Note: MVC-COV1901 refers to MVC COVID-19 vaccine; AZD-1222 refers to Vaxzevria vaccine.

Abbreviations: N = number of participants in the population; n = number of participants with available data; GMT = geometric mean titre; CI = confidence interval; PPI = per protocol immunogenicity analysis set; GMTR = geometric mean titre treatment ratio.

Note: blood samples on Day 1 for immunogenicity test were collected before the administration of study intervention. GMT ratio was compared to Day 1 (prior to first dose).

1 GMT treatment ratio (GMTR) = $\frac{\text{GMT MVC-COV 1901}}{\text{GMT AZD1222}}$ at Day 43 (14 days after second dose).

2 P-value based on two sample t test or Wilcoxon rank sum test.

For the first 225 subjects the GMT for neutralising antibodies induced by MVC was superior to Vaxzervria when assessed 14 days after the second dose of vaccine (Table 3).

Table 4: Study CT-COV-31 Geometric mean titres and geometric mean titre ratio of antigen specific immunoglobulin at Baseline and Visit 4/Day 43 (immunogenicity and per protocol immunogenicity analysis set) (in BAU/mL)

Visit	Statistics	MVC-COV1901	AZD1222	GMTR (MVC/AZ) [1]	*p*-value [2]
All Participants in the Immunogenicity Analysis Set, N		**444**	**440**		
Day 1 (Prior to 1st dose)	n	444	440		
	GMT	20.4	24.9	0.82	0.064
	95% CI of GMT	(17.8-23.5)	(21.5-28.7)		
Day 43 (14 days after 2nd dose)	n	444	440		
	GMT	1916.6	848.6	2.3	<0.001
	95% CI of GMT	(2752.8-2095.6)	(751.2-958.7)	(1.9-2.6)	
	n	444	440		
	GMT ratio	93.8	34.1	2.8	<0.001
	95% CI of GMT ratio	(79.5-220.8)	(28.2-41.2)	(1.9-2.6)	
Subgroup: Seronaive in Immunogenicity Analysis Set, N		**180**	**146**		
Day 1 (Prior to 1st dose)	n	180	146		
	GMT	4.6	4.6	1	-
	95% CI of GMT	(4.6-4.6)	(4.6-4.6)		
Day 43 (14 days after 2nd dose)	n	180	146		
	GMT	1091.8	231.5	4.7	<0.001
	95% CI of GMT	(945.7-1260.5)	(196.7-272.4)	(3.8 – 5.9)	
	n	180	146		
	GMT ratio	239.4	50.8	4.7	<0.001
	95% CI of GMT ratio	(207.5-276.3)	(43.2-59.7)	(3.8 – 5.9)	

Note: MVC-COV1901 refers to MVC COVID-19 vaccine; AZD-1222 refers to Vaxzevria vaccine.

Abbreviations: BAU/mL = Binding Antibodies Units; N = number of participants in the population; n = number of participants with available data; GMT = geometric mean titre; CI = confidence interval; PPI = per protocol immunogenicity analysis set; GMTR = geometric mean titre treatment ratio.

Seroconversion based on neutralising antibody titres was greater than 90% in both arms of the trial but was statistically higher in the MVC COVID-19 vaccine to the Vaxzervria vaccine group (99.1% versus 91.7%, p = 0.008) (seeTable 4). The TGA's clinical evaluation has noted that MVC COVID-19 vaccine was not statistically superior to Vaxzervria in the sub-set of subjects who were sero-naive at enrolment.

Based on the entire population available in the final clinical study report (n = 884), there appeared to be superior induction of antigen specific antibodies using MVC COVID-19 vaccine to Vaxzervria at 14 days after the second dose of vaccine.

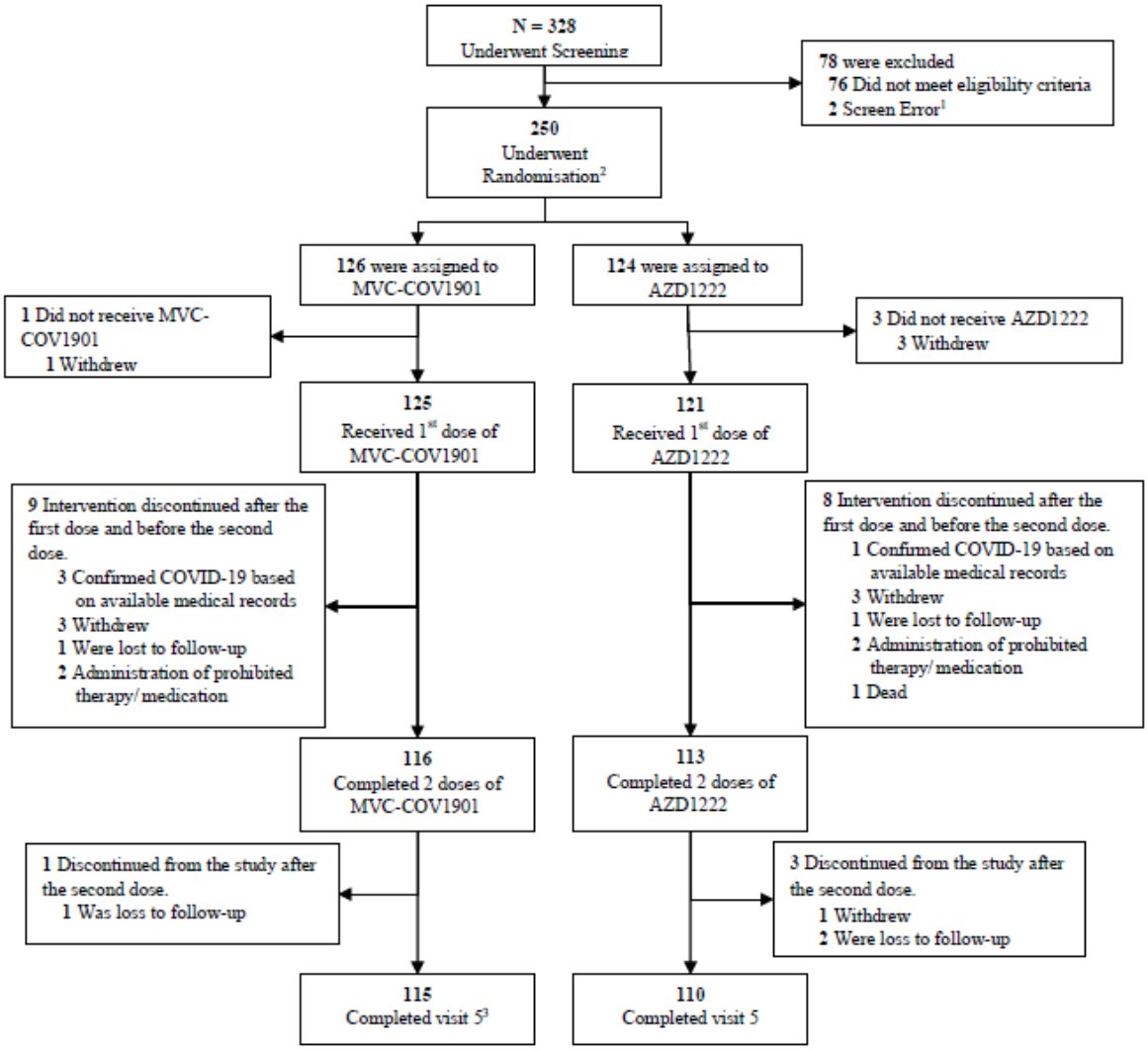
Study CT-COV-32

This was a Phase III study that compared the immunogenicity of the MVC COVID-19 vaccine and the Vaxzervria vaccine in 250 randomised adult subjects. Subjects were randomised to receive the MVC COVID-19 vaccine (n = 125) or Vaxzervria (n = 121) in two dose schedule 28 days apart.

The primary endpoints were:

- The GMT of neutralising antibodies measured at 14 days after the second dose of vaccine. The objective was to demonstrate superiority of MVC COVID-19 vaccine to Vaxzervria.
- Seroconversion (4 fold increase in neutralising antibody titre). The objective was to demonstrate non-inferiority of MVC COVID-19 vaccine to Vaxzervria.

Figure 2: Study CT-COV-32 Patient disposition



Note: MVC-COV1901 refers to MVC COVID-19 vaccine; AZD-1222 refers to Vaxzevria vaccine.

Note: The '2 Screen Error' refers to subjects who were eligible to participate in the study but did not enter study due to randomisation quota being used up.

The study population was older than Study CT-COV-31, with a median age of 55.9 years. The majority were seronegative for neutralising antibodies at Baseline (95.9%). A significant proportion (38.6%) of subjects had positive anti-N antibodies at Baseline (see Figure 2).

Table 5: Study CT-COV-32 Geometric mean titre and geometric mean titre ratio of wild type neutralising antibodies at Day 43 in full analysis set

Visit	Statistics	MVC-COV1901 (N = 125)	AZD1222 (N = 121)	GMTR GMT(MVC-COV1901)/ GMT(AZD1222) 95% CI [a]	P-value [b]
Visit 2 (Day1)	n [c]	125	121		
	Median (Min, Max)	4.0(4.0,158.5)	4.0(4.0,39.8)		
	Q1, Q3 (IQR)	4.0,4.0(0.0)	4.0,4.0(0.0)		
	GMT (95% CI)	4.4(4.1,4.8)	4.1(3.9,4.2)	-	-
Visit 4 (Day 43)	n [c]	116	111		
	Median (Min, Max)	89.1(4.0,501.2)	39.8(4.0,354.8)		
	Q1, Q3 (IQR)	44.7,158.5(113.8)	20.0,89.1(69.2)		
	GMT (95% CI)	69.5(56.3,85.6)	35.7(28.3,45.1)	1.9(1.4,2.7)	<0.001(w)
	n [c]	116	111		
	GMT Ratio (95% CI) [d]	16.0(12.8,20.0)	8.9(7.1,11.3)		

Note: MVC-COV1901 refers to MVC COVID-19 vaccine; AZD-1222 refers to Vaxzevria vaccine.

Abbreviations: N = number of participants in the full analysis set; n = number of participants with available data; Q1 = first quartile (25th percentile); Q3 = third quartile (75th percentile); IQR = interquartile range; GMTR = geometric mean titre treatment ratio; GMT = geometric mean titre; CI = confidence interval; FAS = full analysis set.

The study found that MVC COVID-19 vaccine was superior to Vaxzervria vaccine based on the ratio of GMT for neutralising antibodies, 1.9 (95% confidence interval: 1.4 to 2.7) at 14 days post vaccination (Table 5).

Table 6: Study CT-COV-32 Antigen specific immunoglobulin titres at Day 1, 29 and 43 in the per protocol population

Visit	Statistics	MVC-COV1901 (N = 75)	AZD1222 (N = 73)	GMTR GMT(MVC-COV1901)/ GMT(AZD1222) 95% CI [a]	P-value [b]
Visit 2 (Day 1)	n [c]	75	73		
	Median (Min, Max)	100.0(100.0,161.0)	100.0(100.0,452.0)		
	Q1, Q3 (IQR)	100.0,100.0(0.0)	100.0,100.0(0.0)		
	GMT (95% CI)	101.9(99.9,103.9)	104.8(99.1,110.8)	1.0(0.9,1.0)	0.779(w)
Visit 3 (Day 29)	n [c]	68	71		
	Median (Min, Max)	243.5(100.0,5803.0)	572.0(100.0,9336.0)		
	Q1, Q3 (IQR)	130.5,543.0(412.5)	278.0,1169.0(891.0)		
	GMT (95% CI)	309.6(241.3,397.2)	574.9(444.7,743.2)	0.5(0.4,0.8)	<0.001(w)
	GMT ratio (95% CI)[d]	3.0(2.4,3.9)	5.5(4.2,7.1)		
	P-value (x)[e]	<0.001	<0.001		
Visit 4 (Day 43)	n [c]	64	65		
	Median (Min, Max)	7665.5(100.0,86110.0)	1608.0(100.0,35005.0)		
	Q1, Q3 (IQR)	4192.0,19545.5(15353.5)	827.0,4310.0(3483.0)		
	GMT (95% CI)	8465.9(6219.3,11523.9)	1786.4(1312.5,2431.3)	4.7(3.1,7.3)	<0.001(w)
	GMT ratio (95% CI)[d]	83.0(61.1,112.8)	16.9(12.4,23.1)		
	P-value (x)[e]	<0.001	<0.001		

Note: MVC-COV1901 refers to MVC COVID-19 vaccine; AZD-1222 refers to Vaxzevria vaccine.

Abbreviations: AZD1222 = Vaxzervria, N = number of participants in the per protocol set at Visit 2; n = number of participants in the PPS which is determined by each visit ; 1 = first quartile (25th percentile); Q3 = third quartile (75th percentile); IQR = interquartile range; GMT = geometric mean titre; GMTR = geometric mean titre treatment ratio; CI = confidence interval PPS = per protocol set.

The seroconversion rate was 90% for the MVC COVID-19 vaccine and 82.3% for the Vaxzervria vaccine at 14 days post vaccination, which met non-inferiority criteria; note the reduced numbers, as shown in Table 6 (above).

An exploratory analysis of cell mediated immunity was performed on a subset of subjects (n = 21) using an ELISpot assay.

> 'In the CMI population [exploratory immunogenicity subset to examine cell-mediated immunity], mean baseline IL-4 values were comparable between the treatment groups (0.3 ± 0.48 SFC/10^6 PBMC [peripheral blood mononuclear cells] in the MVC-COV1901 group versus 0.9 ± 2.35 SFC/10^6 PBMC in the AZD1222 [Vaxzevria vaccine] group, p = 0.55). At Visit 4/Day 43, mean values increased to 2.1 ± 3.94 SFC/10^6 PBMC in the MVC-COV1901 group, and remained constant in the AZD1222 group (0.9 ± 1.82 SFC/10^6 PBMC), without difference between the 2 treatment arms (P = 0.7). No difference was observed between the groups in IL-4 mean change from Baseline to Visit 4 (1.8 ± 3.83 SFC/10^6 PBMC versus 0.0 ± 1.6 SFC/10^6 PBMC, p = 0.55, respectively)
>
> Interferon (IFN) gamma responses between Visit 2 and Visit 4 for the CMI and PP-CMI population [exploratory immunogenicity and per protocol subset to examine cell mediated immunity] are provided in sponsor submitted dossier.
>
> In the CMI population, mean baseline IFN-gamma values were comparable between the treatment groups (1.9 ± 3.05 SFC/10^6 PBMC in the MVC-COV1901 group versus 2.7 ± 2.26 SFC/10^6 PBMC in the ADZ1222 group, p = 0.36). At Visit 4/Day 43, mean values increased to 6.0 ± 6.52 SFC/10^6 PBMC in the MVC-COV1901 group, and 5.8 ± 4.85 SFC/10^6 PBMC, without difference between the 2 treatment arms (P = 0.5). No difference was observed between the groups in IFN-gamma mean change from Baseline to Visit 4 (4.1 ± 5.68 SFC/10^6 PBMC versus 3.1 ± 4.24 SFC/10^6 PBMC, p = 0.53, respectively).'

Source: transcribed from clinical study report, CT-COV-32.

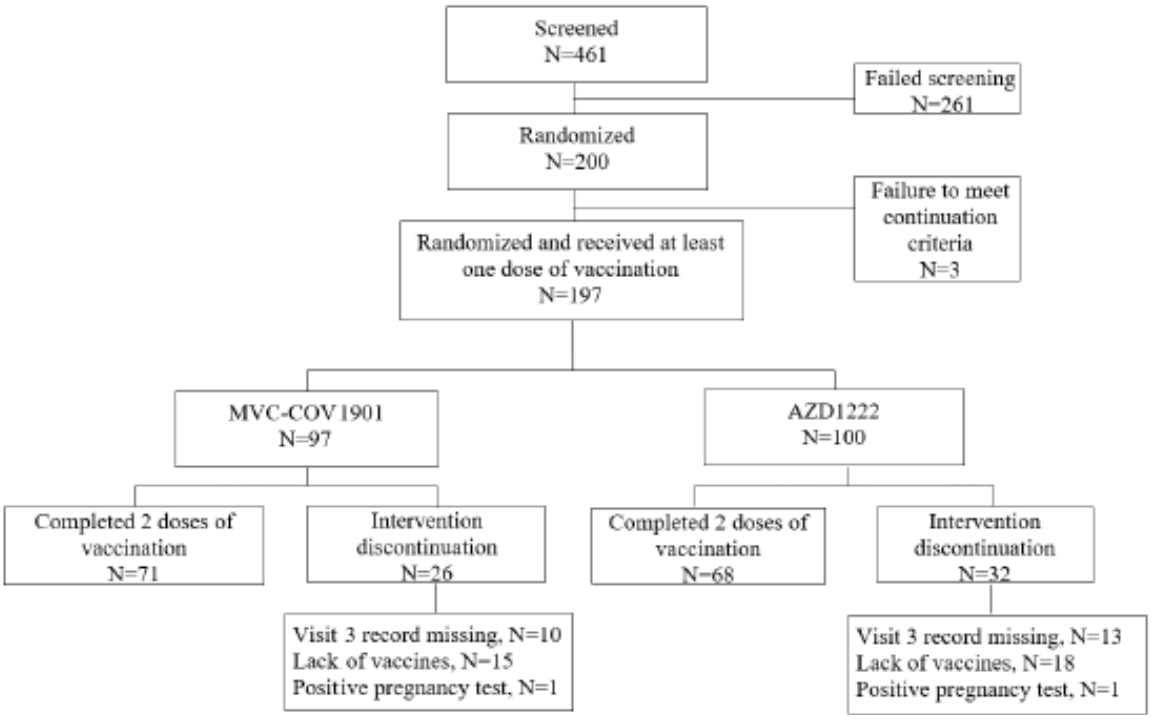
Study CT-COV-34

Study CT-COV-34 was a Phase III comparison of MVC COVID-19 vaccine to Vaxzervria vaccine conducted in adults.

The primary endpoints were:

- The GMT of neutralising antibodies measured at 14 days after the second dose of vaccine. The objective was to demonstrate superiority of MVC COVID-19 vaccine to Vaxzervria.
- Seroconversion (4-fold increase in neutralising antibody titre). The objective was to demonstrate non-inferiority of MVC COVID-19 vaccine to Vaxzervria.

Figure 3: Study CT-COV-34 Patient disposition



The mean age of participants was 32.3 years. A large percentage of subjects had neutralising antibodies at Baseline (79.7%), but most (99.5%) had negative anti-N antibodies on rapid antigen testing at Baseline. The Delegate notes that previous vaccination was an exclusion criterion for this trial (Figure 3).

Table 7: Study CT-COV-34 Geometric mean titre of wild-type neutralising antibodies at Day 43

Visit	Statistics	MVC-COV1901 N=97	AZD1222 N=100	GMT ratio (MVC/AZD1222)	P-value [1]
Day (Vaccination 1)	n	97	100		
	GMT	50.14	38.43	1.30	0.2180
	95% CI of GMT	(37.58,66.89)	(28.12,52.53)	(0.85,1.99)	
Day 43	n	69	69		
	GMT	230.02	227.50	1.03	0.8819
	95% CI of GMT	(184.09,287.41)	(175.24,295.34)	(0.73,1.43)	
	n	69	69		
	GMT ratio [2]	4.70	5.45		
	95% CI of GMT ratio	(3.44,6.44)	(3.94,7.56)		

Note: MVC-COV1901 refers to MVC COVID-19 vaccine; AZD-1222 refers to Vaxzevria vaccine.

Abbreviations: N = number of subjects in the population; n = number of subjects with available data; GMT = geometric mean titre; CI = confidence interval

Note: Blood sample for immunogenicity test are collected before administration of study intervention.

1 P value based on general linear model including the Ln (titres) as the dependent variable, the vaccine group as the independent variable and the age group as a covariate.

2 GMT ratio compared to Day 1 (pre-vaccination).

The study found no significant increase in GMT for neutralising antibodies in MVC COVID-19 vaccine recipients compared to Vaxzervria vaccine recipients at 14 days after the second dose of vaccine. The evaluator has noted that the numbers in this study were smaller than in other studies.

The seroconversion rate was 49.3% for MVC COVID-19 vaccine and 63.8% for Vaxzervria vaccine following two doses, that is a GMT rise of greater than 4 times from Baseline (Table 7).

The clinical evaluator requested further information from the sponsor regarding this low seroconversion rate. The sponsor has indicated that this was due to the high pre-existing sero-positivity in this trial in which was 84.5% in the MVC COVID-19 vaccine group. The sponsor has indicated that this made achieving a four-fold increase in titre difficult.

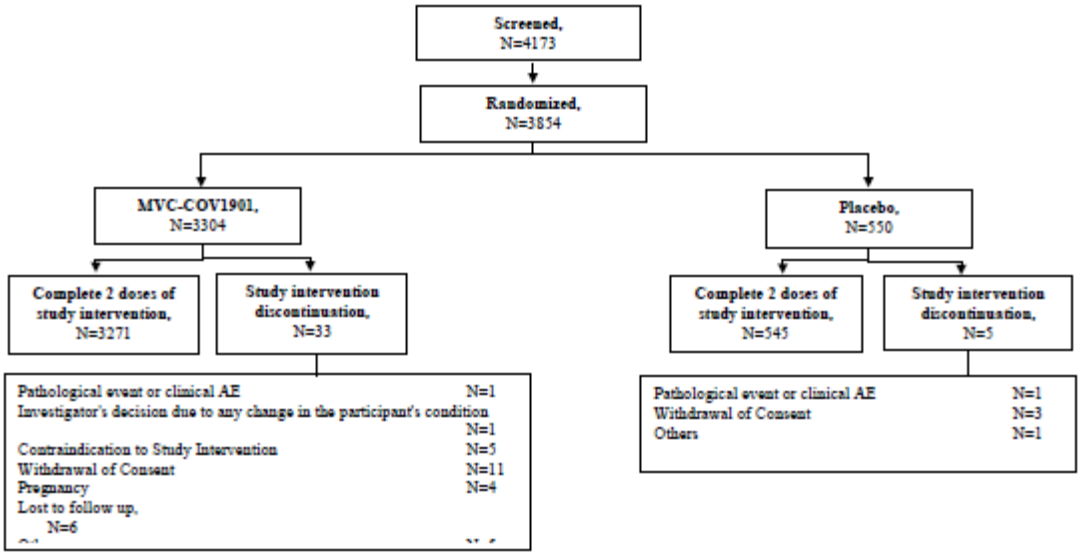
Study CT-COV-21

Study CT-COV-21 was a large placebo controlled Phase II trial intended to examine the safety and immunogenicity of MVC COVID-19 vaccine in healthy subjects. Included were adults between over 20 years of age, who received two doses of vaccine or placebo at Days 0 and 28 (Figure 4).

This study is of significant interest to this submission as it provided the adult comparators for immune response used in the adolescent study, Study CT-COV-22.

Immunogenicity was assessed at 28 days post the second dose of treatment (Day 57).

Figure 4: Study CT-COV-21 Disposition of participants



Note: MVC-COV1901 refers to MVC COVID-19 vaccine

The average age of the subjects was 44.9 years with a near equal gender balance. The majority of subjects (99%) were seronegative for neutralising antibodies against SARS-CoV-2, but anti-nucleocapsid status was not reported (Figure 4).

Table 8: Study CT-COV-21 Geometric mean titres of wild-type neutralising antibodies at Day 57

Visit	Statistics	MVC-COV1901	Placebo	Ratio (MVC/Placebo)	*P*-value [1]
All Participants in the PPI Subset, N		**903**	**150**		
Day 1 (Prior to First dose)	n	903	150		
	GMT	4.06	4.02	1.01	0.2406
	95% CI of GMT	(4.02, 4.09)	(3.98, 4.07)	(0.99, 1.02)	
Day 57	n	903	150		
	GMT	662.31	4.00	165.58	<0.0001
	95% CI of GMT	(628.66, 697.75)	(4.00, 4.00)	(157.16, 174.44)	
	n	903	150		
	GMT ratio	163.22	0.99	164.15	<0.0001
	95% CI of GMT ratio	(155.01, 171.87)	(0.98, 1.01)	(155.71, 173.05)	
Subgroup: ≥ 20 to < 65 years of age, N		**682**	**113**		
Day 1 (Prior to first dose)	n	682	113		
	GMT	4.06	4.03	1.01	0.4119
	95% CI of GMT	(4.02, 4.11)	(3.97, 4.09)	(0.99, 1.03)	
Day 57	n	682	113		
	GMT	732.89	4.00	183.22	<0.0001
	95% CI of GMT	(692.41, 775.74)	(4.00, 4.00)	(173.10, 193.94)	
	n	682	113		
	GMT ratio	180.45	0.99	181.82	<0.0001
	95% CI of GMT ratio	(170.59, 190.89)	(0.98, 1.01)	(171.55, 192.70)	
Subgroup: ≥ 65 years of age, N		**221**	**37**		
Day 1 (Prior to First Dose)	n	221	37		
	GMT	4.05	4.00	1.01	0.1730
	95% CI of GMT	(3.98, 4.11)	(4.00, 4.00)	(0.99, 1.03)	
Day 57	n	221	37		
	GMT	484.54	4.00	121.14	<0.0001
	95% CI of GMT	(433.16, 542.01)	(4.00, 4.00)	(108.29, 135.50)	
	n	221	37		
	GMT ratio	119.75	1.00	119.75	<0.0001
	95% CI of GMT ratio	(107.16, 133.82)	(1.00, 1.00)	(107.16, 133.82)	

Note: MVC-COV1901 refers to MVC COVID-19 vaccine

Abbreviations: N = number of participants in the population; n = number of participants with available data; GMT = geometric mean titre; CI = confidence interval.

Note: Blood samples on Day 1 for immunogenicity test were collected before the administration of study intervention. GMT ratio was compared to Day 1 (prior to first dose).

1 p-value based on two sample t test or Wilcoxon rank sum test.

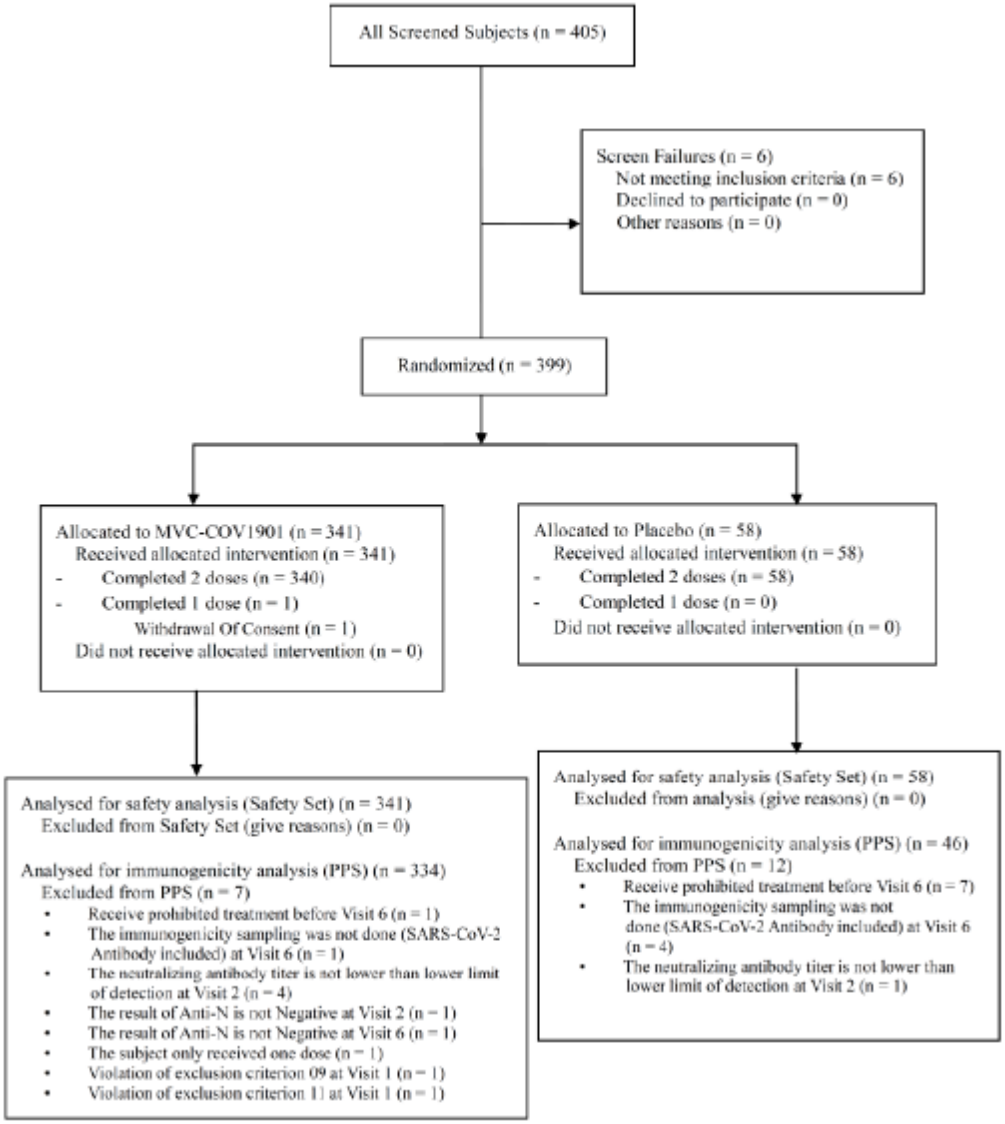
The study found a significant increase in GMT for neutralising antibodies at Day 57 in subjects who received MVC (Table 8).

This corresponded to a seroconversion rate of 99.8% overall, with no difference between the 682 subjects younger than 65 years of age (99.9%) and the 221 subjects greater than 65 years of age (99.5%).

Study CT-COV-22

Study CT-COV-22 was a Phase II study conducted in healthy subjects between the ages of 12 and 18 years of age.

Figure 5: Study CT-COV-22 Patient disposition



Subjects were randomised to receive either MVC COVID-19 vaccine or placebo in a two-dose schedule administered at Day 0 and 28 (Figure 5)

The primary immunogenicity endpoint was anti-spike GMT at Day 57 (28 days post-Dose 2).

Immunogenicity in adults was compared with young adults immunogenicity endpoints from Study CT-COV-21, which was a similar Phase II study conducted in young adults 20 to 30 years of age.

The objective was to establish non-inferiority for the adolescent group to the young adult group based on the ratio of GMT for adolescents/adults of greater than 0.66.

Table 9: Study CT-COV-22 Geometric mean titres of wild type neutralising antibodies

Wild-type Virus Neutralization Geometric Mean Titer	PPS			
	Adolescents of MVC-COV1901	Young Adults of MVC-COV1901	Ratio §Adole/§Young	P-value
Titer at Visit 6				
N (Missing)	334 (0)	210 (0)	-	-
Median (IQR)	1024.0 (980.4)	724.1 (803.1)		
Q1 ~ Q3	645.1 ~ 1625.5	645.1 ~ 1448.2		
Min ~ Max	173.4 ~ 7022.5	203.2 ~ 10321.3		
GMT [t]	1032.842	898.149	1.150	0.0161★T test
95% CI of GMT [t]	960.5891 ~ 1110.529	824.3884 ~ 978.5097	**1.0264** ~ 1.2884T	
GMT [w]	1024.000	724.080	1.173	0.0045★Wilcox_z
95% CI of GMT [w]	879.9300 ~ 1149.400	724.0800 ~ 812.7500	**1.0000** ~ 1.2968HL	

Note: MVC-COV1901 refers to MVC COVID-19 vaccine.

1 For CI (WT, within group), t denotes by using one sample t-test, w denotes CI of median

2 For CI and p-value (between groupds), T denotes two sample t test, Wilcox z denotes Wilcoxon rank-sum test in normal approximation, HL denotes CI using Hodges-Lehman for median

3 For groups diff, § Adole = adolescents of MVC-COV1901, § Young = young adults of MVC-COV1901, T = Student t

4 For p-value,★denotes significant at level 0.05.

At 28 days post-Dose 2 the GMT for the adolescent group and the adult group was essentially equivalent and within the pre-stated margins of non-inferiority (Table 9). The clinical evaluator has noted that this was a comparison across two different studies rather than within a study protocol, albeit with similar protocols.

Safety

No dedicated safety studies were submitted.

Data from controlled studies was short term and mainly recorded reactogenic adverse events.

There is a significant body of post-marketed adverse event reporting from the use of MVC in Taiwan, which was provided following TGA's questions posed to the sponsor following the first round of clinical evaluation.

Table 10: Study CT-COV-31 Solicited adverse events by symptom and severity

Solicited Systemic AEs Time point, Severity	n (%)		
	MVC-COV1901 N=520 (N=466 for 2nd dose)	AZD1222 N=510 (N=459 for 2nd dose)	Total N=1030 (N=925 for 2nd dose)
Any Solicited Systemic AEs			
After Any Dose, All severity	**225 (49.0)**	**295 (57.8)**	**550 (53.4)**
After First Dose, All severity	**212 (40.8)**	**259 (50.8)**	**471 (45.7)**
After Second Dose, All severity	**114 (24.5)**	**113 (24.6)**	**227 (24.5)**
Headache			
After Any Dose, All severity	**146 (28.1)**	**192 (37.6)**	**338 (32.8)**
Grade 1	136 (26.2)	166 (32.5)	302 (29.3)
Grade 2	31 (6.0)	45 (8.8)	76 (7.4)
Grade 3	5 (1.0)	10 (2.0)	15 (1.5)
After First Dose, All severity	**116 (22.3)**	**165 (32.4)**	**281 (27.3)**
Grade 1	106 (20.4)	142 (27.8)	248 (24.1)
Grade 2	21 (4.0)	36 (7.1)	57 (5.5)
Grade 3	2 (0.4)	10 (2.0)	12 (1.2)
After Second Dose, All severity	**60 (12.9)**	**59 (12.9)**	**119 (12.9)**
Grade 1	53 (11.4)	53 (11.5)	106 (11.5)
Grade 2	14 (3.0)	9 (2.0)	23 (2.5)
Grade 3	3 (0.6)	1 (0.2)	4 (0.4)
Myalgia			
After Any Dose, All severity	**117 (22.5)**	**167 (32.7)**	**284 (27.6)**
Grade 1	110 (21.2)	152 (29.8)	262 (25.4)
Grade 2	21 (4.0)	40 (7.8)	61 (5.9)
Grade 3	6 (1.2)	4 (0.8)	10 (1.0)
After First Dose, All severity	**86 (16.5)**	**150 (29.4)**	**236 (22.9)**
Grade 1	79 (15.2)	132 (25.9)	211 (20.5)
Grade 2	13 (2.5)	37 (7.3)	50 (4.9)
Grade 3	1 (0.2)	4 (0.8)	5 (0.5)
After Second Dose, All severity	**52 (11.2)**	**39 (8.5)**	**91 (9.8)**
Grade 1	47 (10.1)	34 (7.4)	81 (8.8)
Grade 2	10 (2.1)	7 (1.5)	17 (1.8)
Grade 3	5 (1.1)	0 (0.0)	5 (0.5)
Malaise/Fatigue			
After Any Dose, All severity	**107 (20.6)**	**141 (27.6)**	**248 (24.1)**
Grade 1	101 (19.4)	126 (24.7)	227 (22.0)
Grade 2	23 (4.4)	32 (6.3)	55 (5.3)
Grade 3	3 (0.6)	5 (1.0)	8 (0.8)
After First Dose, All severity	**75 (14.4)**	**115 (22.5)**	**190 (18.4)**
Grade 1	71 (13.7)	99 (19.4)	170 (16.5)
Grade 2	15 (2.9)	28 (5.5)	43 (4.2)
Grade 3	2 (0.4)	2 (0.4)	4 (0.4)

Table 12 (continued): Study CT-COV-31 Solicited adverse events by symptom and severity

After Second Dose, All severity	**53 (11.4)**	**45 (9.8)**	**98 (10.6)**
Grade 1	50 (10.7)	41 (8.9)	91 (9.8)
Grade 2	12 (2.6)	7 (1.5)	19 (2.1)
Grade 3	1 (0.2)	3 (0.7)	4 (0.4)
Joint Pain			
After Any Dose, All severity	**59 (11.3)**	**91 (17.8)**	**150 (14.6)**
Grade 1	53 (10.2)	87 (17.1)	140 (13.6)
Grade 2	12 (2.3)	20 (3.9)	32 (3.1)
Grade 3	2 (0.4)	4 (0.8)	6 (0.6)
After First Dose, All severity	**41 (7.9)**	**77 (15.1)**	**118 (11.5)**
Grade 1	40 (7.7)	71 (13.9)	111 (10.8)
Grade 2	3 (0.6)	16 (3.1)	19 (1.8)
Grade 3	1 (0.2)	4 (0.8)	5 (0.5)
After Second Dose, All severity	**23 (4.9)**	**23 (5.0)**	**46 (5.0)**
Grade 1	15 (3.2)	22 (4.8)	37 (4.0)
Grade 2	10 (2.1)	5 (1.1)	15 (1.6)
Grade 3	1 (0.2)	0 (0.0)	1 (0.1)
Fever			
After Any Dose, All severity	**41 (7.9)**	**75 (14.7)**	**116 (11.3)**
Grade 1	27 (5.2)	48 (9.4)	75 (7.3)
Grade 2	7 (1.3)	18 (3.5)	25 (2.4)
Grade 3	7 (1.3)	16 (3.1)	23 (2.2)
Grade 4	1 (0.2)	0 (0.0)	1 (0.1)
After First Dose, All severity	**24 (4.6)**	**58 (11.4)**	**82 (8.0)**
Grade 1	16 (3.1)	35 (6.9)	51 (5.0)
Grade 2	5 (1.0)	14 (2.7)	19 (1.8)
Grade 3	4 (0.8)	11 (2.2)	15 (1.5)
After Second Dose, All severity	18 (3.9)	26 (5.7)	44 (4.8)
Grade 1	12 (2.6)	18 (3.9)	30 (3.2)
Grade 2	2 (0.4)	6 (1.3)	8 (0.9)
Grade 3	3 (0.6)	5 (1.1)	8 (0.9)
Grade 4	1 (0.2)	0 (0.0)	1 (0.1)
Chills			
After Any Dose, All severity	**40 (7.7)**	**77 (15.1)**	**117 (11.4)**
Grade 1	38 (7.3)	67 (13.1)	105 (10.2)
Grade 2	8 (1.5)	12 (2.4)	20 (1.9)
Grade 3	2 (0.4)	4 (0.8)	6 (0.6)
After First Dose, All severity	**25 (4.8)**	**68 (13.3)**	**93 (9.0)**
Grade 1	24 (4.6)	59 (11.6)	83 (8.1)
Grade 2	6 (1.2)	10 (2.0)	16 (1.6)
Grade 3	0 (0.0)	4 (0.8)	4 (0.4)
After Second Dose, All severity	**21 (4.5)**	**15 (3.3)**	**36 (3.9)**
Grade 1	19 (4.1)	14 (3.1)	33 (3.6)
Grade 2	3 (0.6)	2 (0.4)	5 (0.5)
Grade 3	2 (0.4)	0 (0.0)	2 (0.2)

Table 10 (continued): Study CT-COV-31 Solicited adverse events by symptom and severity

Nausea			
After Any Dose, All severity	**60 (11.5)**	**51 (10.0)**	**111 (10.8)**
After First Dose, All severity	**44 (8.5)**	**41 (8.0)**	**85 (8.3)**
After Second Dose, All severity	**19 (4.1)**	**16 (3.5)**	**35 (3.8)**
Diarrhea			
After Any Dose, All severity	**39 (7.5)**	**44 (8.6)**	**83 (8.1)**
After First Dose, All severity	**26 (5.0)**	**29 (5.7)**	**55 (5.3)**
After Second Dose, All severity	**14 (3.0)**	**16 (3.5)**	**30 (3.2)**

Abbreviations: AE = adverse event; N = number of participants in the population, n = number of participants in the specific category

Note: Percentages of participants were calculated with N as the denominator. For each time period, the number and percentage of participants who experienced any of the individual solicited AEs by the highest severity were presented.

In Study CT-COV-31 the percentage of systemic adverse events after the first dose was 45.7% and after the second was 24.5% in recipients of MVC COVID-19 vaccine. The most common adverse events were pain/tenderness (33.1%), which was comparable between MVC COVID-19 vaccine and Vaxzervria. Headache, fever, malaise and myalgia were relatively common with MVC COVID-19 vaccine administration, but occurred at lower rates than Vaxzervria (Table 10).

There was one death in an adult in Study CT-COV-21 due to respiratory failure, which was considered unrelated to vaccine. In the adolescent population (Study CT-COV-22) the rate of solicited adverse events (AEs) observed was similar to that in adults, but with a higher rate of local pain/tenderness (69.8%) after the first dose at a mild grade of severity (Table 11). Overall 47.5% of the MVC COVID-19 vaccine and 44.8% of the placebo group experienced at least one solicited systemic AEs

No serious adverse events, vaccine associated enhanced disease or adverse events of special interest were reported.

There was no significant pattern amongst the un-solicited AEs.

Table 11: Study CT-COV-22 Solicited adverse events by symptom and severity in adolescents

Solicited AEs	MVC-COV1901	Placebo	Total
After Any Vaccination			
N	**341**	**58**	**399**
At least one below [Event#:Subj#]	773: 265 (77.7%)	83: 31 (53.4%)	856: 296 (74.2%)
~ Max. Grade 1	225 (66.0%)	26 (44.8%)	251 (62.9%)
~ Max. Grade 2	38 (11.1%)	5 (8.6%)	43 (10.8%)
~ Max. Grade 3	2 (0.6%)	0	2 (0.5%)

After Vaccination 2			
N	**340**	**58**	**398**
At least one below	312: 182 (53.5%)	37: 16 (27.6%)	349: 198 (49.7%)
~ Max. Grade 1	155 (45.6%)	12 (20.7%)	167 (42.0%)
~ Max. Grade 2	25 (7.4%)	4 (6.9%)	29 (7.3%)
~ Max. Grade 3	2 (0.6%)	0	2 (0.5%)

Solicited AEs	MVC-COV1901	Placebo	Total
Local Reaction	**169: 163 (47.9%)**	**14: 14 (24.1%)**	**183: 177 (44.5%)**
~ Any	169: 163 (47.9%)	14: 14 (24.1%)	183: 177 (44.5%)
~ Max. Grade 1	148 (43.5%)	13 (22.4%)	161 (40.5%)
~ Max. Grade 2	15 (4.4%)	1 (1.7%)	16 (4.0%)
~ Pain/Tenderness	162: 162 (47.6%)	14: 14 (24.1%)	176: 176 (44.2%)
~ Grade 1	148: 148 (43.5%)	13: 13 (22.4%)	161: 161 (40.5%)
~ Grade 2	14: 14 (4.1%)	1: 1 (1.7%)	15: 15 (3.8%)
~ Induration/Swelling	5: 5 (1.5%)	0	5: 5 (1.3%)
~ Grade 1	3: 3 (0.9%)	0	3: 3 (0.8%)
~ Grade 2	2: 2 (0.6%)	0	2: 2 (0.5%)
~ Erythema/Redness	2: 2 (0.6%)	0	2: 2 (0.5%)
~ Grade 1	2: 2 (0.6%)	0	2: 2 (0.5%)
Systemic Reaction	**143: 86 (25.3%)**	**23: 12 (20.7%)**	**166: 98 (24.6%)**
~ Any	143: 86 (25.3%)	23: 12 (20.7%)	166: 98 (24.6%)
~ Max. Grade 1	66 (19.4%)	8 (13.8%)	74 (18.6%)
~ Max. Grade 2	18 (5.3%)	4 (6.9%)	22 (5.5%)
~ Max. Grade 3	2 (0.6%)	0	2 (0.5%)
~ Malaise/Fatigue	63: 63 (18.5%)	8: 8 (13.8%)	71: 71 (17.8%)
~ Grade 1	54: 54 (15.9%)	6: 6 (10.3%)	60: 60 (15.1%)
~ Grade 2	8: 8 (2.4%)	2: 2 (3.4%)	10: 10 (2.5%)
~ Grade 3	1: 1 (0.3%)	0	1: 1 (0.3%)
~ Headache	27: 27 (7.9%)	6: 6 (10.3%)	33: 33 (8.3%)
~ Grade 1	23: 23 (6.8%)	3: 3 (5.2%)	26: 26 (6.5%)
~ Grade 2	3: 3 (0.9%)	3: 3 (5.2%)	6: 6 (1.5%)
~ Grade 3	1: 1 (0.3%)	0	1: 1 (0.3%)
~ Myalgia	28: 28 (8.2%)	4: 4 (6.9%)	32: 32 (8.0%)
~ Grade 1	21: 21 (6.2%)	3: 3 (5.2%)	24: 24 (6.0%)
~ Grade 2	7: 7 (2.1%)	1: 1 (1.7%)	8: 8 (2.0%)
~ Diarrhea	18: 18 (5.3%)	2: 2 (3.4%)	20: 20 (5.0%)

Solicited AEs	MVC-COV1901	Placebo	Total
~ Grade 1	15: 15 (4.4%)	2: 2 (3.4%)	17: 17 (4.3%)
~ Grade 2	3: 3 (0.9%)	0	3: 3 (0.8%)
~ Nausea/Vomiting	6: 6 (1.8%)	3: 3 (5.2%)	9: 9 (2.3%)
~ Grade 1	4: 4 (1.2%)	2: 2 (3.4%)	6: 6 (1.5%)
~ Grade 2	2: 2 (0.6%)	1: 1 (1.7%)	3: 3 (0.8%)
~ Fever	1: 1 (0.3%)	0	1: 1 (0.3%)
~ Grade 1	1: 1 (0.3%)	0	1: 1 (0.3%)

Markers of potential myocarditis were examined in the pharmacodynamic studies, Studies CT-COV-11 and CT-COV-25. There was one possibly related Grade 1 ECG abnormality reported but no cases of myocarditis reported in these studies.

In Studies CT-COV-11 and CT-COV-25 platelet count, coagulation time and activated partial thromboplastin time were conducted at Baseline, Day 15, 29, 43 and 57. No abnormalities of clotting function were detected in patients in these trials.

Post-market data on safety

The sponsor has noted that in the complete clinical trial data set to 29 March 2023 (n = 5945), which post-dates this submission by several months, there have been no cases of vaccine-induced immune thrombotic thrombocytopenia, myocarditis, Guillain-Barre syndrome or anaphylaxis reported.

There has been significant use of the MVC COVID-19 vaccine in Taiwan which provides post-marketing data through pharmacovigilance reporting to the Taiwan Food and Drug Administration. A summary of adverse event reports from 3,069,255 doses of MVC COVID-19 vaccine administered is provided in Table 12.

Table 12: Taiwan Food and Drug Administration; Estimates of rates of adverse events of special interest from adverse event notification during deployment of MVC COVID-19 vaccine

Risk Term	Current analytical process
Myocarditis/Pericarditis (Covid-19 vaccine AESI)	Category: **Potential risk** Three (3) reported cases are confirmed vaccinated with MVC COVID-19 Vaccine by Taiwan National ADR Reporting Center. Incidence rate: **0.97 cases per million doses** *OE analysis: **OE ratio ≦ 1.**
Thrombosis with thrombocytopenia syndrome (TTS) (Covid-19 vaccine AESI)	Category: **Potential risk** One (1) reported case is confirmed vaccinated with MVC COVID-19 Vaccine by Taiwan National ADR Reporting Center. Incidence rate: **0.33 cases per million doses** *OE analysis: **Not available.**
Cerebral venous sinus thrombosis (CVST) without thrombocytopenia	Category: **Potential risk** One (1) reported case is confirmed vaccinated with MVC COVID-19 Vaccine by Taiwan National ADR Reporting Center. Incidence rate: **0.33 cases per million doses** *OE analysis: **OE ratio ≦ 1.**
Idiopathic Thrombocytopenic Purpura (ITP) (Covid-19 vaccine AESI)	Category: **Potential risk** Zero (0) reported cases have been confirmed vaccinated with MVC COVID-19 Vaccine by Taiwan National ADR Reporting Center. Incidence rate: **0 cases per million doses** *OE analysis: **OE ratio ≦ 1.**
Guillain–Barre´ Syndrome (GBS) (Covid-19 vaccine AESI)	Category: **Potential risk** Two (2) reported cases have been confirmed vaccinated with MVC COVID-19 Vaccine by Taiwan National ADR Reporting Center. Incidence rate: **0.65 cases per million doses** *OE analysis: **OE ratio ≦ 1.**
Severe allergic reactions including anaphylaxis (Covid-19 vaccine AESI)	Category: **Important potential risk** Six (6) anaphylaxis reported case is confirmed vaccinated with MVC COVID-19 Vaccine by Taiwan National ADR Reporting Center, later announced by TFDA. Incidence rate: **1.95 cases per million doses** *OE analysis: **OE ratio > 1.**

Abbreviations: OE = observed-expected analyses are conducted by the Taiwan Food and Drug Administration and announced weekly.

* OE analysis are conducted by Taiwan Food and Drug Administration and announced weekly.

Table 13: Taiwan COVID-19 immunisation data; Comparison of rates of adverse event of special interest observed in with MVC COVID-19 vaccine and other licensed COVID-19 vaccines

Incidences per million doses	AZD1222	mRNA-1273	MVC-COV1901	BNT162b2
Thrombosis with thrombocytopenia syndrome	3.46	0.08	0.33	0.00
Cerebral venous sinus thrombosis without throm	1.18	0.33	0.33	0.20
Myocarditis/pericarditis	1.50	7.33	0.98	11.87
Guillain-Barre Syndrome	1.24	0.54	0.65	0.15
Idiopathic thrombocytopenic purpura	3.01	0.88	0.00	0.56
Anaphylaxis	1.63	0.67	1.95	0.15

Abbreviations: AZD1222 = Vaxzevria COVID-19 vaccine (Astra-Zeneca); BNT162b2 = Comirnaty COVID-19 vaccine (Pfizer); MVC-COV1901 = MVC COVID-19 vaccine; mRNA-1273 = Spikevax COVID-19 vaccine (Moderna)

In comparison to reports received for other vaccines used in Taiwan, the rate of rare adverse event of special interest for the MVC COVID-19 vaccine appears to have lower rates except for severe allergic reactions (Table 13). It has a low rate of myocarditis reported. However, the Delegate notes that the Emergency Usage Authorisation reported in 2022 for the MVC COVID-19 vaccine in Taiwan was for adults and this excludes the highest risk cohorts for myocarditis.

Risk management plan

The sponsor has submitted European Union (EU)-RMP version 0.1 (dated 25 April 2022; data lock point (DLP) 30 March 2022) and Australia specific annex (ASA) version 0.1 (dated 28 April 2022) in support of this application. The sponsor has provided EU-RMP version 0.2 (dated 7 October 2022; DLP 30 September 2022) and ASA version 0.2 (dated 13 October 2022) in response to TGA's questions. At third round of evaluation, sponsor has provided EU-RMP version 0.3 (dated 25 November 2022; DLP 25 November 2022) and ASA version 0.3 (dated 1 December 2022).

The summary of safety concerns and their associated risk monitoring and mitigation strategies are summarised in Table 14. The TGA may request an updated RMP at any stage of a product's life-cycle, during both the pre-approval and post-approval phases.

Table 14: Summary of safety concerns

Summary of safety concerns		Pharmacovigilance		Risk Minimisation	
		Routine	Additional	Routine	Additional
Important identified risks	None	–	–	–	–
Important potential risks	Myocarditis/Pericarditis	✓	✓1	✓	–
	Severe allergic reactions including anaphylaxis	✓2	✓1	✓	–
	Vaccine-associated enhanced disease (VAED), including vaccine-associated enhanced respiratory disease (VAERD)	✓2	✓1	–	–
Missing information	Children below 12 years of age	✓	–	✓	–
	Use in pregnancy and while breast-feeding	✓	✓3	✓	–
	Interaction with other vaccines	✓	–	✓	–

Summary of safety concerns		Pharmacovigilance		Risk Minimisation	
		Routine	Additional	Routine	Additional
	Use in frail subjects with unstable health conditions and co-morbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders)	✓	–	–	–
	Use in immunocompromised subjects	✓	✓[1]	✓	–
	Use in patients with autoimmune disorders or inflammatory disorders	✓	–	✓	–
	Long-term safety	✓	✓[1]	–	–

[1] Clinical trials

[2] Follow-up questionnaires

[3]Pregnancy registry

Subject to comments from the clinical and nonclinical evaluators, the summary of safety concerns is considered acceptable from an RMP perspective.

The sponsor was requested to provide clarification on the additional pharmacovigilance activities, amend the follow-up questionnaires and provide a clinical study plan. In the response to TGA questions, the ASA has been updated with a clinical study plan and amended follow-up questionnaires. At third round of evaluation, sponsor has updated the ASA to remove discrepancies about the additional pharmacovigilance activities. Further editorial amendment has been requested at the next ASA update. Overall, the pharmacovigilance plan is acceptable.

Only routine risk minimisation activities have been proposed and this approach is acceptable. The draft PI and Consumer Medicines Information (CMI) have been amended as requested and the Risk minimisation plan is acceptable.

Proposed wording for conditions of registration

Any changes to which the sponsor has agreed should be included in a revised RMP and ASA. However, irrespective of whether or not they are included in the currently available version of the RMP document, the agreed changes become part of the risk management system.

> 'The MVC COVID-19 Vaccine EU-Risk Management Plan (RMP) (version 0.3, dated 25 November 2022, data lock point 25 November 2022), with Australia Specific Annex (version 0.3, dated 1 December 2022), included with submission PM-2022-011101-1-2, to be revised to the satisfaction of the TGA, and any subsequent revisions, will be implemented in Australia.
>
> An obligatory component of risk management plans is routine pharmacovigilance. Routine pharmacovigilance includes the submission of periodic safety update reports (PSURs).
>
> Unless agreed separately between the supplier who is the recipient of the approval and the TGA, the first report must be submitted to TGA no later than 15 calendar months after the date of the approval letter. The subsequent reports must be submitted no less frequently than annually from the date of the first submitted report until the period

covered by such reports is not less than three years from the date of the approval letter, or the entire period of provisional registration, whichever is longer.

The reports are to at least meet the requirements for PSURs as described in the European Medicines Agency's Guideline on good pharmacovigilance practices (GVP) Module VII-periodic safety update report (Rev 1), Part VII.B Structures and processes. Note that submission of a PSUR does not constitute an application to vary the registration. Each report must have been prepared within ninety calendar days of the data lock point for that report.

Additional to the routine submission of the routine PSURs, expedited monthly safety summary reports (including safety data for patients in Australia) are to be provided for **the 6 months from the date of first supply in Australia**, and thereafter at intervals specified by the TGA.

MVC COVID-19 Vaccine (SARS-CoV-2 rS (MVC-COV1901)) is to be included in the Black Triangle Scheme. The PI and CMI for MVC COVID-19 Vaccine must include the black triangle symbol and mandatory accompanying text for five years, or the product's entire period of provisional registration, whichever is longer.'

Risk-benefit analysis

Delegate's considerations

The sponsor has provided several Phase III trials which demonstrate induction of serological immunity 14 to 28 days after a two dose schedule of MVC COVID-19 vaccine administered at Days 0 and 28 in subjects 12 years and older. There is no vaccine efficacy data, and the immunogenicity is validated against wild type SARS-CoV-2 infection. The Delegate notes that this limits the applicability of the results in these trials to contemporary use of the vaccine against Omicron and future SARS-CoV-2 strains. The one study (Study CT-COV-25) which did explore immunogenicity against variants of concern, including Omicron, used a three or four dose schedule of vaccination and so the Delegate does not consider the results to be applicable to the proposed primary schedule of two doses.

Clinical efficacy

Clinical validation of the efficacy of MVC within the trial dossier relies on a head to head comparison with the Vaxzevria vaccine in Studies CT-COV-31, -32 and -34. However, the primary endpoints of seroconversion and GMT ratio for neutralising antibodies in these studies was measured 14 days after the second dose of vaccine. While this provides provisional evidence of comparative efficacy, it provides no evidence of the duration of immunity expected from MVC. The Delegate notes that the protocol for Study CT-COV-31 has visits to Day 209 post vaccination and these immune endpoints at six months would be valuable in forming an assessment of the overall utility of the MVC COVID-19 vaccine. The Delegate also notes that while the Vaxzevria vaccine can be administered as two doses over 4 weeks, the optimal dosage interval is 12 weeks. The Delegate considers, therefore, that the non-inferiority of the MVC COVID-19 vaccine to Vaxzevria vaccine may not be valid for prospective vaccination outside of an epidemic in which shorter intervals are necessary to achieve rapid population immunity.

Information provided by the Taiwan Food and Drug Regulator provides useful observational data regarding efficacy. Within a limited cohort of patients who had only received two doses of vaccine between 2021 and 2022 in Taiwan, the vaccine efficacy of the MVC COVID-19 vaccine against COVID-19 disease and death appeared similar to Vaxzevria. The MVC COVID-19 vaccine

was clearly less effective than two doses of mRNA vaccine and provided moderate levels of protection that was lower in older recipients. This dataset did not contain any adolescent data.

Effect of prior exposure of the trial recipients to SARS-CoV-2

The Delegate notes that in Studies CT-COV-31 and -32 a significant proportion of subjects had anti-nucleocapsid antibodies at Baseline, which indicates prior infection with COVID. Prior infection may influence the immune response achieved following vaccination by acting as a natural 'booster'. In Study CT-COV-31, for example, the GMT for neutralising antibodies in the MVC COVID-19 vaccine group was 1087.8 after dose two in the overall population, and 434.6 in the sero-naïve subpopulation. This analysis does not appear to have been performed in Study CT-COV-32.

The Delegate notes that in Study CT-COV-34 the population was almost universally anti-nucleocapsid negative, but also 80% neutralising antibody positive at Baseline. This would suggest the population was vaccinated prior to baseline, which clearly shouldn't be the case. However, it makes the interpretation of the results of this study difficult.

Cell mediated immunity

There is limited exploratory analysis of the stimulation of cell mediated immunity by MVC vaccine, but where this has been examined in Study CT-COV-32 it provides some evidence of cellular recruitment. While this is helpful, the Delegate notes that correlating these findings to long term protection would require clinical outcome studies.

Adolescent population

The serological response achieved in adolescents in Study CT-COV-22 appears similar to that in younger adults in Study CT-COV-21. This analysis is potentially flawed by it being across two different trial populations with, potentially, different rates of pre-existing exposure to SARS-CoV-2. However, the Delegate feels that it provides a reasonable basis for extrapolating the use of the MVC COVID-19 vaccine into this group.

Safety

All of the clinical studies submitted are short term and so there is limited controlled data regarding the safety of the MVC COVID-19 vaccine. This is largely reactogenicity data, which the TGA Delegate feels is fairly unremarkable for a COVID vaccine. There is, however, considerable post-market experience with this vaccine and the sponsor has provided data from pharmacovigilance reporting to the Taiwan FDA. While the emergence of a new rare adverse events cannot be excluded from the current data, the observed rates of known severe adverse events of COVID vaccination (for example, vaccine induced immune thrombotic thrombocytopenia, anaphylaxis, myocarditis, and so on) appear to be within the rates observed with other products. The MVC COVID-19 vaccine may have a benefit in causing lower rates of myocarditis, which would suggest a potential role in adolescents.

Provisional status

The Delegate notes that the requirements for provisional registration under the Therapeutic Goods Act (1990) are as follows:

Therapeutic Goods Act (1990)

(d) for an application for provisional registration of a medicine:

(i) whether based on preliminary clinical data, the safety and efficacy of the medicine for the purposes for which it is to be used have been satisfactorily established; and

(ii) whether the quality of the medicine for the purposes for which it is to be used has been satisfactorily established; and

(iii) whether, if the Secretary were to register the medicine, the Secretary is satisfied with the applicant's plan to submit comprehensive clinical data on the safety and efficacy of the medicine before the end of the 6 years that would start on the day that registration would commence.

The data provided is certainly preliminary in that there is no long term immunogenicity data or vaccine efficacy data. Whether this constitutes a satisfactory establishment of efficacy for the MVC COVID-19 vaccine may depend somewhat on the clinical and historical context of its proposed use. Short term data was accepted for vaccines early in the COVID pandemic because achieving immunity in a sero-naïve population was a priority. However, most vaccines in use have now demonstrated a degree of long term protection more appropriate for use protecting vulnerable individuals in populations where COVID-19 is endemic.

Proposed action

At the time, the Delegate was minded to provisionally register the MVC COVID-19 vaccine for the proposed indication, pending the advice of Advisory Committee on Vaccines (ACV). The sponsor should note that the Delegate will consider the view of ACV to be determinative in relation to this submission.

Any decision to register the MVC COVID-19 vaccine is conditional on:

1. The sponsor resolving outstanding quality requirements, particularly GMP for manufacturing sites, satisfactorily.
2. The sponsor providing details of an updated study plan detailing when studies will be submitted to TGA to transition to full registration.
3. The sponsor providing a PI document annotated to indicate amendments as recommended by the RMP, pre-clinical and (where applicable) quality evaluators.

Advisory Committee considerations

The Advisory Committee on Vaccines (ACV), having considered the evaluations and the Delegate's overview, as well as the sponsor's response to these documents, advised the following.

Specific advice to the Delegate

1. Is the preliminary data provided sufficient to support the provisional registration of MVC COVID-19 vaccine?

The ACV advised that the preliminary data were not sufficient to support provisional registration of a two-dose schedule of the MVC COVID-19 vaccine.

Clinical data demonstrated induction of short term immunological response 14 days after a two-dose schedule administered 28 days apart in subjects aged 18 years and older that was not inferior to the comparator vaccine [Vaxzevria].

Against these benefits, the ACV highlighted the following points:

- No long-term immunogenicity data were presented relevant to the proposed two-dose schedule.
- Immunogenicity following the two-dose schedule was demonstrated only against wild-type strain of SARS-CoV-2.
- Immunogenicity data were not stratified for prior infection in all studies.
- Clinical trial data did not provide any clinical vaccine efficacy assessment, and while the observational vaccine effectiveness data suggested that a two-dose vaccine schedule may have been moderately effective early in the pandemic against severe COVID-19 from the ancestral virus, this virus is no longer in circulation.
- There were limited clinical trial data in adolescents (approximately 300 individuals), which were potentially flawed by reliance on cross-study comparisons, and there were no post-market data for this age group.
- All studies were in healthy subjects or people with stable chronic disease.
- The novel adjuvant does not have a sufficient safety profile.

The ACV noted that real-world data suggested that a third dose of MVC COVID-19 vaccine appeared to substantially improve vaccine effectiveness, however a three-dose schedule was not proposed by the sponsor.

The ACV advised that it did not support a first provisional registration (compared to renewal of provisional registration) of a COVID-19 vaccine with clinical trial data only on immunogenicity and only against the ancestral strain of SARS-CoV-2.

Should the Delegate proceed to approve the vaccine, the ACV advised that the indication should:

- allow use for individuals 18 years and older;
- be similar in form to that used for other COVID-19 vaccines (for example, to require use in accordance with official guidelines); and
- state that the decision has been made 'on the basis of short-term immunogenicity data (against the ancestral strain) and safety data'

Conclusion

The proposed indication considered by the ACV was:

> *'This vaccine has provisional approval in Australia for active immunisation to prevent novel coronavirus disease (COVID-19, also known as severe pneumonia with novel pathogens) in individuals 12 years of age and older.*

The decision to approve this indication has been made on the basis of safety, immunogenicity, and efficacy data in completed and ongoing clinical trials and immunobridging studies. Continued approval of this indication depends on verification and description of benefit in confirmatory trials and post-market assessment.

This vaccine should be administered in accordance with the COVID-19 vaccination plan of the Central Epidemic Command Centre.'

Explanation:

The indications are based on the neutralising antibody titre being comparable in amount, after two doses of the vaccine, to import products that have received special approval for use.'

The ACV agreed that the MVC COVID-19 vaccine did not have a clear benefit-risk profile sufficient for provisional registration for the proposed indication as the evidence submitted did not satisfactorily establish the quality, safety and efficacy of the vaccine within the context of the current circulating SARS-CoV-2 virus variants.

Outcome

The sponsor withdrew their submission on 25 July 2023 before a decision had been made by the TGA. The sponsor expressed their intention to resubmit the application as a three-dose schedule.

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Reference/Publication #