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Experience of the United Arab Emirates in the use of monoclonal antibody drug sotrovimab in high-risk vaccinated and unvaccinated patients with COVID-19: an observational cohort study

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ABSTRACT

Objectives Monoclonal antibodies can slow COVID-19 progression. This study describes the experience of using sotrovimab in patients with COVID-19 at high risk for disease progression and hospitalisation within the United Arab Emirates (UAE).

Design Observational cohort study.

Setting A tertiary hospital in the Emirate of Sharjah, UAE.

Participants Patients with mild or moderate COVID-19 at high risk for disease progression.

Interventions Infusion with a single 500 mg dose of the monoclonal antibody drug sotrovimab.

Primary and secondary outcome measures Any adverse effect within 24 hours, disease progression within 5 days, emergency department visit within 10 days, hospital admission within 10 days or mortality within 28 days of infusion.

Results 3227 high-risk COVID-19 patients were infused with sotrovimab during the mild (n=3107, 96.3%) or moderate (n=120, 3.7%) disease stages. The incidence of at least one outcome was recorded in 196 (6.1%) of the patients (60.7 per 1000 patients). The most common outcome was disease progression within 5 days of infusion in 129 patients (4.0%), followed by emergency department visits by 90 patients (2.8%) within 10 days. Twenty-nine (0.9%) patients were hospitalised within 10 days of infusion with only two deaths (0.1%). Patients infused with sotrovimab during the moderate disease stage had 11 times greater odds of developing at least one outcome compared with patients infused during the mild stage (adjusted OR, aOR 10.86, 95% CI 7.14 to 16.54). SARS-CoV-2 vaccinated (aOR 12.8, 95% CI 7.3 to 20.5) and unvaccinated (aOR 7.2, 95% CI 3.4 to 15.3) patients infused with sotrovimab during the moderate disease stage had similar odds of at least one outcome compared with patients infused during the mild stage.

Conclusions Among high-risk sotrovimab-infused COVID-19 patients, there were relatively low incidences of disease progression and hospitalisation. Regardless of vaccination history, monoclonal antibody intervention during the early stages of COVID-19 results in better outcomes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study followed a standardised protocol to identify eligible patients and to administer the monoclonal antibody drug sotrovimab.
⇒ The study applied a standardised definition to measure all investigated outcomes.
⇒ The study opens a window for future research into the use of monoclonal antibodies in patients exempted from vaccination.
⇒ The lack of a comparison group of patients, who did not receive sotrovimab, imposes limitations on the observed findings; however, this limitation was unavoidable given the mandate to infuse all eligible patients with sotrovimab.
⇒ The multiplicity of confounders might also be a limitation; however, it is inventible in observational studies with ethical obligations to treat all eligible patients.

INTRODUCTION

Since the first reports of COVID-19 and the identification of the novel SARS-CoV-2, the infection has spread to more than 634 million confirmed cases and caused over 6.62 million deaths worldwide as of 21 November 2022.[1] Over time, SARS-CoV-2 mutations have resulted in the emergence of new variants and subvariants with variable transmissibility, severity, infectivity and degrees of respiratory manifestations.[2] The pandemic remains ongoing and is fuelled by the emergence of new variants and subvariants.

The health, economic and social burdens of disease are devastating, especially with the severe infection pattern of SARS-CoV-2. In 16 European countries, the total Disability-Adjusted Life-Years (DALYs) that resulted from the COVID-19 pandemic accounted for 4354 per 100.000 inhabitants, and the years of

life lost were accountable for 98% of those total DALYs.[3] In New York, USA, the estimated average years of potential life lost in New York state and New York City was 12.72 and 15.31 years per person, and the estimated value of statistical life was US$119.62 and US$90.45 billion, respectively.[4] The COVID-19 pandemic was also associated with several mental health problems, including panic attacks, impulsivity, depression and anxiety disorders, suicidal behaviour, sleep disorders and emotional disturbance.[5] Patients with signs and symptoms of COVID-19 are classified according to symptoms as mild, moderate, severe or critical. The mild disease stage is defined as individuals who have any symptoms of COVID-19 (eg, fever, cough, sore throat, malaise, headache, loss of taste and smell) but without dyspnoea or abnormal chest imaging. The moderate stage is defined as individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have a peripheral oxygen saturation (SpO_2) level of ≥94% on room air at sea level. The severe disease stage is defined as individuals who have SpO_2<94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxyge (PaO_2/FiO_2) <300 mm Hg, respiratory frequency >30 breaths/min or lung infiltrates >50%. Progression to critical illness is defined by respiratory failure, septic shock and/or multiple organ dysfunction.[6]

Patients diagnosed with COVID-19 and at high risk of progression to the severe form of the disease need intervention with highly effective protocolised therapeutics to avoid adding more burdens and complexities to the healthcare system. It is intuitive to use new tools to prevent disease progression. One promising tool to prevent progression is the use of neutralising monoclonal antibodies. Neutralising monoclonal antibody therapies targeting SARS-CoV-2 have been found to accelerate the reduction in viral loads and reduce the risk of disease progression for outpatients with mild COVID-19.[7–12] Sotrovimab is an engineered human monoclonal antibody designed to neutralise SARS-CoV-1 and SARS-CoV-2 viruses with possible efficacy against mutant strains and variants of the same viruses.[13] In our practice, therapy with sotrovimab was started in 2021 after emergency authorisation was granted for outpatients with mild COVID-19 as a tool to prevent disease progression.[14] This study describes the incidence of adverse effects within 24 hours, disease progression within 5 days, emergency department visits within 10 days, hospitalisation within 10 days and mortality within 28 days of infusion with sotrovimab in a cohort of ambulatory patients who presented with early symptomatic COVID-19 and were at high risk for disease progression and hospitalisation, in the United Arab Emirates (UAE).

METHODS

This observational cohort study was conducted between 14 November 2021 and 31 January 2022, at the Al Qassimi Hospital, a tertiary healthcare centre of the Emirates Health Services in the Emirate of Sharjah. After reviewing the protocol proposed for the emergency use authorisation of sotrovimab, a sotrovimab administration protocol for outpatient use was developed (online supplemental file 1). This study included all patients infused with sotrovimab during the study period.

Study population

Following our protocol (online supplemental file 1), high-risk patients eligible for infusion with sotrovimab were defined as high-risk patients who had a positive reverse-transcriptase-PCR (RT-PCR) for SARS-CoV-2 or its antigen. COVID-19 patients confirmed through RT-PCR as eligible to receive sotrovimab needed to present with a mild or moderate disease stage and should have been at high risk for progression to a severe form of COVID-19.

Eligibility criteria for infusion with sotrovimab

Inclusion criteria

Patients were considered high risk if they were aged ≥65 years with or without any comorbidities. Additionally, patients aged <65 years with comorbidities were considered high-risk patients. Comorbidities included diabetes mellitus, cardiovascular disease (eg, congenital heart disease, hypertension, congestive heart failure), chronic lung disease (eg, chronic obstructive pulmonary disease, moderate to severe asthma, interstitial lung disease, cystic fibrosis and pulmonary hypertension), immunocompromising conditions or those receiving immunosuppressive treatment, chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m^2 of body-surface area), sickle cell disease, neurodevelopmental disorders (eg, cerebral palsy) or other conditions that confer medical complexity (eg, genetic or metabolic syndromes and severe congenital anomalies, dependence on artificial support (eg, tracheostomy, gastrostomy or positive pressure ventilation not related to COVID-19). Pregnant women were also considered as high-risk COVID-19 patients.

Exclusion criteria

Patients with antigen or RT-PCR confirmed COVID-19 were not eligible to receive sotrovimab if they presented with a severe form of COVID-19, were already hospitalised, were aged <13 years, had a body mass index (BMI) less than 25 kg/m^2 and/or had no other risk factors such as chronic comorbidities.

Disease severity

The levels of disease severity that determined exclusion or inclusion in the study were defined as mild, moderate, severe or critical illness. A patient with mild illness was defined as any patient who presented with any of the various signs and symptoms of COVID-19 (eg, fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea or loss of taste and smell) but who did not have dyspnoea or abnormal chest imaging. A patient with moderate illness was defined as any patient who presented with evidence of lower respiratory disease during clinical assessment or imaging and who had

Table 1 Frequency occurrence and incidence of the five measured outcomes during follow-up

Measured outcome	Frequency (%)	Incidence
Any of the measured five outcomes (n=3213)	196 (6.1)	60.7 per 1000 patients
Any adverse effect within 24 hours (n=3223)		10.8 per 1000 patients
Yes	35 (1.1%)	
No	3188 (98.9%)	
Disease progression within 5 days (n=3226)		40.0 per 1000 patients
Yes	129 (4.0%)	
No	3097 (96.0%)	
Emergency department visit within 10 days (n=3216)		27.9 per 1000 patients
Yes	90 (2.8%)	
No	3126 (97.2%)	
Hospital admission within 10 days (n=3227)		
Yes	29 (0.9%)	9.0 per 1000 patients
No	3198 (99.1%)	
Mortality within 28 days (n=3220)		6.2 per 10 000 patients
Yes	2 (0.1%)	
No	3218 (99.9%)	

SpO_2≥94% on room air at sea level. A patient with severe illness was defined as one with SpO_2<94% on room air at sea level, a ratio of PaO_2/FiO_2 <300 mm Hg, a respiratory rate>30 breaths/min or lung infiltrates >50%. Patients with critical illness were defined as individuals who had respiratory failure, septic shock and/or multiple organ dysfunctions.

Intervention and patient care

Eligible patients received a single 500 mg dose of sotrovimab through 1-hour infusion according to the clearly defined roles and responsibilities of the monoclonal antibodies infusion pathway. Once the primary physician decided to refer the patient for monoclonal antibodies infusion therapy, the following data were documented: date of testing COVID-19 positive, the severity of disease, start date of symptoms, history of any allergies, BMI, indication for monoclonal antibodies, and any special health conditions such as pregnancy or lactation.

The monoclonal antibody medications were prepared aseptically and administered with close observation and monitoring of each patient. The rapid response team was prepared to respond to any adverse event. Post-sotrovimab administration, each patient was monitored for hypersensitivity reaction for 60 min following infusion. Patients were discharged with instructions and a telephone hotline number.

Measured outcomes

Five outcome types were measured in the cohort of patients who received sotrovimab infusions. These outcomes included encountering any adverse effect within 24 hours of infusion, disease progression within 5 days of infusion, emergency department visit within 10 days of infusion, hospital admission within 10 days of infusion or mortality within 28 days of infusion. Hospitalisation was defined as hospital admission for more than 24 hours secondary to either disease progression after receiving sotrovimab or secondary to adverse events related to sotrovimab infusion. Hospitalisations that were related to other illnesses such as fracture or pregnancy follow-ups were excluded to avoid double counting.

The monitored adverse effects that may have been encountered during and after sotrovimab infusion included fever, difficulty breathing, low oxygen level, chills, tiredness, fast or slow heart rate, chest discomfort or pain, weakness, confusion, nausea, headache, dyspnoea, low or high blood pressure, wheezing, swelling of lips, face or throat, rash including hives, itching, muscle aches, dizziness, feeling faint and sweating.

Statistical analysis

The measured patients' sociodemographic and medical characteristics at the time of sotrovimab infusion were described. Categorical characteristics were described using frequency and proportion. Normally distributed continuous variables were described using measures of central tendency, mean and SD. The median and IQR were provided for the non-normal distributed variables. The normality assumption was verified using the Shapiro-Wilk test. The occurrence (yes, no) of each of the five measured binary outcomes was reported as frequency and proportion.

Since patients who, for example, experienced disease progression are likely to visit the emergency room as well as to be hospitalised, the five measured outcomes were recategorised into one binary outcome. This was done to avoid duplicate counting of the measured outcomes for the same patient. This binary outcome covered the occurrence (yes, no) of any of the five measured outcomes. The incidence rate of this binary outcome and encounters with any of the five measured outcomes were then reported by the measured characteristics at the time of sotrovimab infusion per 1000 or 10 000 patients, when applicable.

Crude and multivariable logistic regression models were used to investigate the association between the measured characteristics and the occurrence of any of the five measured outcomes. The modification effect resulting from patient SARS-CoV-2 vaccination status on the association between some measured characteristics and the occurrence of any of the five measured outcomes was also explored.

Table 2 Demographic and medical characteristics at time of sotrovimab infusion, and distribution and incidence of the measured outcomes during follow-up

Characteristics	All=3227 n (valid %)	Any of the outcomes occurred		P value	Incidence of any outcome per 1000 patients
		Yes n=196 (6.1%)	No n=3031 (93.9%)		
Age, median, IQR (range, mean±SD)–year	51.0, 39–62 (11–101, 50.8±15.3)	53.73±15.94	50.16±15.22	0.004*	–
11–30	286 (8.9)	12 (6.1)	274 (9.0)	0.124†	42.0
31–40	607 (18.8)	29 (14.8)	578 (19.1)		47.8
41–60	1390 (43.1)	87 (44.4)	1303 (43.0)		62.6
> 60	944 (29.3)	68 (34.7)	876 (28.9)		72.0
Gender				0.123†	
Male	1 564 (48.2)	84 (42.9)	1470 (48.5)		53.7
Female	1 671 (51.8)	112 (57.1)	1559 (51.5)		67.0
Missing	2				
Pregnancy—females of childbearing age (18–49 years) (n=778)					
Pregnant	56 (7.2)	3 (2.7)	53 (8.0)	0.476	53.6
Not pregnant	722 (92.7)	109 (97.3)	613 (92.0)		150.9
Missing	1				
Nationality or ethnic group				0.800	
Asian, non-Arab	917 (28.4)	56 (28.6)	861 (28.4)		61.1
Arab	2 171 (67.3)	134 (68.4)	2037 (67.2)		61.7
European (19), American (2) or Canadian (9)	30 (0.9)	1 (0.5)	29 (1.0)		33.3
African, non-Arab	91 (2.8)	5 (2.6)	86 (2.8)		54.9
Unknown	18 (0.6)	0 (0.0)	18 (0.06)		0.0
Concurrent chronic comorbidity					
No comorbidity	980 (30.4)	45 (23.1)	935 (30.9)		45.9
Diabetes mellitus	1469 (45.6)	89 (45.6)	1380 (45.5)	0.976	60.6
Cardiovascular disease	1551 (48.1)	113 (57.9)	1438 (47.5)	0.004	72.9
Chronic Kidney Disease	208 (6.5)	15 (7.7)	193 (6.4)	0.468	72.1
Chronic lung disease	287 (8.9)	19 (9.7)	268 (8.8)	0.669	66.2
Immunosuppressive disease	157 (4.9)	12 (6.2)	145 (4.8)	0.238	76.4
At least one concurrent comorbidity					
Yes	2 243 (69.6)	150 (76.9)	2 093 (69.1)	0.022	66.9
No	980 (30.4)	45 (23.1)	935 (30.9)		45.9
Missing	4				
Vaccination status				0.002	
Vaccinated	2 262 (70.5)	110 (60.1)	2 152 (71.1)		48.6
Unvaccinated	947 (29.5)	73 (39.9)	874 (28.9)		77.1
Missing	20				
BMI–kg/m^2				0.311	
Overweight (25–29.9)	1015 (31.5)	58 (29.6)	957 (31.6)		57.1
Obese class I (30–34.9)	879 (27.2)	60 (30.0)	819 (27.0)		68.3
Obese class II (35.1–39.9)	1005 (31.1)	55 (28.1)	950 (31.3)		54.7
Obese class III (40–49.9)	301 (9.3)	23 (11.7)	278 (9.2)		76.4
Super morbid obese (≥50)	27 (0.8)	0 (0.0)	27 (0.9)		0.0
Disease severity at presentation				<0.001	
Mild	3093 (96.3)	142 (77.6)	2 951 (97.4)		45.9
Moderate	119 (3.7)	41 (22.4)	78 (2.6)		34.5
Missing	17				
Duration of symptoms at presentation, mean±SD (range)	2.8±2.1 (0–15)	2.52±1.67	2.79±2.08	0.033*	
≤3 days	2280 (70.7)	152 (77.6)	2128 (70.2)	0.029	66.7

Continued

Table 2 Continued

Characteristics	All=3227 n (valid %)	Any of the outcomes occurred		P value	Incidence of any outcome per 1000 patients
		Yes n=196 (6.1%)	No n=3031 (93.9%)		
>3 days	946 (29.3)	44 (22.4)	902 (29.8)		46.5
Missing	2				
Duration between PCR positivity and sotrovimab administration, mean±SD (range)	2.1±1.6 (0–6)			0.446	
0–1 day	1723 (53.4)	99 (50.8)	1624 (53.6)		57.5
≥2 days	1503 (46.6)	96 (49.2)	1407 (46.4)		63.9
Missing	3				
Duration between symptoms and sotrovimab administration, mean±SD (range)	3.74±2.3 (0–16)			0.054	
≤2 days	1078 (33.5)	53 (27.2)	1025 (33.9)		49.2
>2 days	2141 (66.5)	142 (72.8)	1999 (66.1)		66.3
Missing	10				

*P value estimated from the non-parametric Mann-Whitney U test for the distribution in two groups.
†P value estimated using the $\chi 2$ test to assess differences in the proportions of outcomes between groups.
BMI, body mass index.

IBM SPSS Statistics V.26 (IBM) was used to perform all analyses. A p<0.05 was considered statistically significant.

Patient and public involvement

Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

RESULTS

Included patients and outcomes occurrence

A total of 3227 high-risk COVID-19 RT-PCR-confirmed patients received sotrovimab infusion following our protocol (online supplemental file 1). Table 1 illustrates the incidence of measured outcomes during follow-up. Of the sotrovimab-infused COVID-19 patients, 196 (6.1% incidence proportion) patients developed at least one of the measured five outcomes that representing an incidence rate of 61 per 1000 patients. The most common occurring outcome was disease progression, which was observed in 129 (4.0%) patients within 5 days of sotrovimab infusion. This was followed by emergency department visits by 90 (2.8%) patients within 10 days. Admission to the hospital within 10 days of sotrovimab infusion occurred in 29 (0.9%) patients, and only two deaths were reported (0.1%) within 28 days of sotrovimab infusion (table 1).

Sociodemographic and medical characteristics

Table 2 shows the measured characteristics distribution at the time of sotrovimab infusion and bivariate associations between these characteristics and the occurrence of at least one of the five measured outcomes. The mean (± SD) patient age was 50.8 (± 15.3) years (range 13–101 years). Approximately, three-quarters (72.4%) of the patients were aged>40 years. The gender distribution of the patients was similar (48.2% male, 51.8% female). Of the 778 childbearing age females, 56 (7.2%) were pregnant. A total of 2259 (70%) patients had at least one chronic comorbidity, with cardiovascular diseases (48.1%) and diabetes mellitus (45.6%) being the two most frequent comorbidities. Of the sotrovimab-infused patients, 952 (29.5%) were not vaccinated against SARS-CoV-2. Overweight patients numbered 1016 (31.5%), while the remainder were different classes of obesity, mainly obesity class II (n=1005, 31.1%). On presentation, 3093 (96.3%) of the sotrovimab-infused patients presented with a mild disease stage. At the time of sotrovimab infusion, 2280 (70.7%) patients were symptomatic for ≤3 days (mean duration of 2.8±2.1 SD), 1723 (53.4%) were PCR positive for ≤1 day (mean duration: 2.1±1.6 SD) and 2141 (66.5%) were symptomatic for >2 days (table 2).

Bivariate association with the development of at least one outcome

The highest observed incidence of at least one of the five outcomes was in patients aged >60 years (72.0 per 1000 patients), with cardiovascular (72.9 per 1000 patients) or immunosuppressive disease (76.4 per 1000 patients), unvaccinated status (77.1 per 1000 patients) and obesity class III (76.4 per 1000 patients) being predominant. Age, having at least one chronic comorbidity (p=0.002), particularly a cardiovascular comorbidity (p=0.004), vaccination status, and duration and severity of symptoms at presentation were significantly associated with developing at least one outcome. The mean patient age (53.7 years) of those who developed at least one outcome was significantly (p=0.004) higher than their counterparts (50.2 years). The occurrence of at least one outcome was significantly (p=0.002) higher among unvaccinated patients (71.1%) compared with those who were vaccinated (60.1%). The proportion of patients who were symptomatic for ≤3 days (77.6%) and developed at least one outcome was higher than patients who were symptomatic for >3 days (22.4%)

Table 3 Bivariable and multivariable association between the measured characteristics at the time of sotrovimab infusion and development of any of the five outcomes measured during follow-up

	OR (95% CI)	Adjusted OR (95% CI)
Age—year	1.01 (1.004 to 1.02), p=0.006	1.007 (1.00 to 1.015, p=0.063)
<60 years	1.00	1.00
≥60 years	1.36 (1.01 to 1.83), p=0.043	1.01 (1.00 to 1.02), p=0.014
Gender		
Male	1.00	–
Female	1.29 (0.96 to 1.73)	–
Nationality or ethnic group		
Asian, non-Arab	1.00	–
Arab	0.98 (0.72 to 1.36)	–
Others	0.68 (0.29 to 1.62)	–
No of concurrent chronic comorbidities		
0	1.00	–
1	1.51 (1.03 to 2.19), p=0.033	–
2	1.36 (0.91 to 2.02), p=0.13	–
3	1.04 (0.50 to 2.16), p=0.919	–
≥4	3.78 (1.50 to 9.46), p=0.005	–
At least one comorbidity	1.44 (1.027 to 2.02), p=0.035	1.36 (0.95 to 1.97), p=0.097
Vaccination status		
Vaccinated	1.00	1.00
Unvaccinated	1.61 (1.19 to 2.19), p=0.002	1.68 (1.22 to 2.30), p=0.001
BMI		
Overweight	1.00	–
Obese class I	1.19 (0.82 to 1.73), p=0.348	–
Obese class II	0.94 (0.64 to 1.37), p=0.745	–
Obese class III or super obese (57 patients)	1.17 (0.71 to 1.94), p=0.543	–
Obese regardless of the obesity class	1.07 (0.78 to 1.47), p=0.657	–
Duration of symptoms at presentation		
>3 days	1.00	1.00
≤3 days	1.51 (107 to 2.13), p=0.020	1.63 (1.13 to 2.36), p=0.009
Symptoms severity		
Mild	1.00	1.00
Moderate	11.29 (7.48 to 17.04), p<0.001	10.86 (7.14 to 16.54), p<0.001
Duration between PCR positivity and sotrovimab administration		
0–1 day	1.00	–
≥2 days	1.11 (0.83 to 1.48), p=0.484	–
Duration between symptoms and sotrovimab administration		
≤2 days	1.00	–
>2 days	1.34 (0.97 to 1.85), p=0.077	–

adjusted OR for age, existence of at least one comorbidity, vaccination status, duration of symptoms at presentation and severity of disease at presentation.
BMI, body mass index.

(incidence rate of 66.7 vs 46.5 per 1000 patients, respectively, p=0.029) (table 2).

Magnitude of association between measured characteristics and development of any designated outcome

The confounder-adjusted analysis revealed that patients aged≥60 years were at 1% increased odds of developing at least one outcome (adjusted OR, aOR 1.01, 95% CI 1.00 to 1.02, p=0.014). Patients who were not vaccinated against SARS-CoV-2 and patients who were symptomatic for ≤3 days had 68% (aOR 1.68, 95% CI 1.22 to 2.30) and 63% (aOR 1.63, 95% CI 1.13 to 2.36) increased odds of developing at least one outcome. In the crude analysis, patients with at least one chronic comorbidity were significantly at 44% increased odds of developing any of the outcomes, but this significant association disappeared when controlled for other variables. Patients infused with sotrovimab during the moderate disease stage at presentation were at 11-time increased odds of developing any of the designated outcomes compared with patients infused with sotrovimab during the mild disease stage (aOR 10.86, 95% CI 7.14 to 16.54, p<0.001) (table 3). This increased odds, while more prominent among the vaccinated (aOR 13.92, 95% CI 8.41 to 23.03) compared with the unvaccinated (aOR 7.66, 95% CI 3.71 to 15.79), was not modified by the vaccination status (overlapping 95% CIs) (table 4). Among the vaccinated, patients infused with sotrovimab ≥2 days of PCR testing positive were at 96% increased odds while unvaccinated patients were at 42% decreased odds of developing any of the outcomes. Additionally, vaccinated patients infused with sotrovimab ≥2 days of being symptomatic were at 2.2-time increased odds of developing any of the designated outcomes (table 4).

DISCUSSIONS

The present observational cohort study monitored the development of five outcomes in high-risk COVID-19 patients who received a sotrovimab infusion to reduce the progression of the disease and prevent severe outcomes. The results of this study describe the UAE's experience in the use of sotrovimab in fighting COVID-19 infections. One of the primary treatment goals was to decrease disease progression and subsequently decrease hospital admission of patients presented at earlier stages of the disease. Older age, disease severity

Table 4 At the time of sotrovimab infusion, crude and adjusted associations between symptom severity, time duration between PCR positivity, and duration of symptoms; with occurrence of at least one of the five measured outcomes in vaccinated and unvaccinated patients

	Vaccinated		Unvaccinated	
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Symptoms severity				
Mild	1.00	1.00	1.00	1.00
Moderate	13.25 (7.98–22.00)*	12.87 (7.31–20.48)*	7.66 (3.71–15.82)*	7.21 (3.40–15.30)*
Duration between PCR positivity and sotrovimab administration				
0–1 day	1.00	1.00	1.00	1.00
≥2 days	1.96 (1.33–2.90)*	1.32 (0.84 to 2.09)	0.58 (0.36 to 0.93)**	0.61 (0.35 to 1.05)
Duration between symptoms and sotrovimab administration				
≤2 days	1.00	1.00	1.00	1.00
>2 days	2.22 (1.41–3.52)*	2.18 (1.25 to 3.78)**	0.94 (0.54 to 1.63)	1.13 (0.61 to 2.21)

aOR for age, gender, BMI, nationality, existence of at least one comorbidity, severity of symptoms, time duration (days) between PCR positivity and sotrovimab administration, and time (days) duration between symptoms and sotrovimab administration.
*p<0.001, **p<0.05.
aOR, adjusted OR; BMI, body mass index.

at presentation and duration of symptoms were linked to having one of the five outcome measures in this study. Additionally, delayed sotrovimab administration during the moderate disease stage was associated with a higher incidence of designated outcomes, regardless of vaccination status.

High rates of COVID-19-related hospitalisation have remained a common concern and are associated with increased mortality rates. These factors require attention to provide support to care for patients in times of increased volume and complexity, such as those experienced during COVID-19 infection peaks. In this study, disease progression was 4.0% and hospital admission within 10 days after sotrovimab administration was 0.9%. In a recent multicentre study, the incidence of COVID-19-related hospitalisation ranged from 2% to more than 25% during pandemic peaks.[15] The observed lower rate of hospitalisation in this study implies the protective effect of sotromivab, particularly since it was administered to patients who were at high risk of disease progression and hospitalisation. Importantly, the effectiveness of single administration or combinations of several monoclonal antibodies to reduce COVID-19-related mortality and hospitalisation has also been discussed and reported in several trials.[8 11 12 16]

The presence of comorbidities associated with risk factors showed no significant increase in outcome events compared with non-comorbid patients. This observation might imply the protective effect incurred by sotrovimab administration. Previous studies have described associations linking intrinsic patient factors such as older age and greater comorbidity with higher in-hospital COVID-19 mortality. Moreover, obesity, liver disease and diabetes were independently associated with increased risk of COVID-19 mortality.[17 18]

Pregnancy is one of the risk factors in the disease course of COVID-19. In this study, the incidence of outcome events among pregnant women was comparable to that in non-pregnant women of childbearing age. In surveillance of over 400 000 persons of reproductive age with symptomatic COVID-19 and adjusted for age, race, ethnicity and underlying medical conditions, non-pregnant women had a 3-time higher likelihood to be admitted to an intensive care unit (10.5 vs 3.9 per 1000 patients), a 2.9-time higher likelihood to require invasive ventilation (2.9 vs 1.1 per 1000 patients), were 2.4-time more likely to require extracorporeal membrane oxygenation (0.7 vs 0.3 per 1000 patients) and were 1.7-time more likely to die (1.5 vs 1.2 per 1000 patients) compared with pregnant women.[19] Similar results were also reported in a European study.[20] In our experience, sotrovimab administration to pregnant women seems to reduce disease progression and severe COVID-19-related outcomes in this high-risk population group. Pregnant women are usually hesitant to receive vaccines given the anecdotal reputation of vaccines impacting offspring. Accordingly, in these circumstances, monoclonal antibody treatment might be a good alternative to vaccines to offer substantial protection from disease.

Vaccination against SARS-CoV-2 is thought to modify the immune response and the level of antibodies against the virus, and the level of neutralising antibodies is highly predictive of the level of protection offered by the immune system.[21 22] In this study, the incidence of at least one of the measured five outcomes was 37% less in vaccinated patients compared with the unvaccinated. However, after crude association within vaccination, patients infused with sotrovimab ≥2 days following PCR testing positive were at a 96% increased risk of developing any of the outcomes, while unvaccinated patients were at

a 42% decreased risk of developing any of the outcomes. Additionally, vaccinated patients infused with sotrovimab ≥2 days of being symptomatic were at a 2.2-time increased likelihood of developing any of the outcomes (table 4). These findings might be explained by the antibody level at the time of treatment with sotrovimab and the modifying effects induced by vaccination on these antibodies. A similar observation was reported earlier in hospitalised patients with COVID-19 who build up endogenous antibodies and were found to receive no benefit from the infusion of neutralising antibodies.[23] The decision whether to refrain from or administer neutralising antibodies, such as sotrovimab, to diseased vaccinated patients should be examined in future studies. In this study, the level of neutralising antibodies was not assessed before the initiation of treatment with sotrovimab. The level of antibodies might be decaying over time in the context of its half-life.[22]

The findings of this study should be interpreted in light of the following acknowledged limitations. The study design lacked a control group of patients with similar characteristics to serve as comparators. Additionally, this study did not investigate the efficacy and safety of sotrovimab as this has been addressed earlier.[16 24] Moreover, there were no data available about the time since the last vaccine dose was received, nor the type and number of vaccine doses received. Data on the history of natural COVID-19 infection was also unavailable. Including high-risk COVID-19 patients from only one centre limits the generalisability of present findings to the wider population of COVID-19 patients. Despite these limitations, this study has several strengths. The study investigated the incidence of outcomes post-sotrovimab administration in a quite large sample population (n=3 227) of high-risk patients with COVID-19. The stratification of patients according to demographics, comorbidity, days since symptom onset, the severity of symptoms and vaccination status, has provided meaningful data. In this study, sotrovimab was administered to both vaccinated and unvaccinated patients early in the course of the disease. Whether disease progression was decelerated by the effect of vaccines or sotrovimab remains unclear in patients who received both medications. However, the incidence of one outcome measure associated with sotrovimab treatment in both groups was <7%. This finding supports the suitability of using monoclonal antibody treatment in cases where vaccination is declined for reasons such as in cases of vaccine hesitancy, medical contraindications to vaccines, immunocompromised persons who may not have a response to a vaccine and the emergence of new viral strains that escape the vaccine-generated immune response. For new evolving variants, sotrovimab was found to have a broad-spectrum protective effect against most of the new strains.[24–26] It is noteworthy that sotrovimab should be used in the early stages of disease in patients which do not satisfy criteria for hospital admission. This is because the drug has shown no benefit after hospitalisation to patients with COVID-19 who developed endogenous antibodies,[23] but there was an observed relatively low incidence of disease progression and hospitalisation in COVID-19 patients infused with sotrovimab during mild or moderate disease stages. Vaccinated patients with symptomatic COVID-19 should be investigated in future studies for eligibility of exogenous treatment with neutralising monoclonal antibodies.

In conclusion, in COVID-19 patients who are at high risk for disease progression and mortality, there was an observed relatively low incidence of disease progression and hospitalisation in COVID-19 patients infused with sotrovimab. To avoid severe COVID-19-related outcomes, early intervention with sotrovimab during the mild disease stage showed a lower incidence of negative outcomes compared with administration during the moderate disease stage, regardless of vaccination status. The vaccinated and unvaccinated patients infused with sotrovimab during the moderate disease stage had similar odds of disease progression and hence admission to the hospital compared with patients infused during their mild disease stage. Hence, regardless of vaccination history, this observation advocates for intervention with monoclonal antibodies in the early stages of COVID-19, as well as the need for robust studies to confirm the present findings.

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