Real-world effectiveness of sotrovimab for the early treatment of COVID-19 in the US

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Background

- Sotrovimab is a dual-action monoclonal antibody that binds to a conserved epitope on the spike protein receptor binding domain of SARS-CoV-2 with both the ability to neutralize the virus as well as recruit the immune system to kill already infected cells *in vitro* and *in vivo*[1,2]
- The COMET-ICE trial (NCT04545060) in patients (n=1057) with mild-to-moderate COVID-19 at high risk of progression to severe disease showed a clinically and statistically significant relative risk reduction (79%; 95% CI: 50%, 91%; $p<0.001$) in all-cause >24-hour hospitalization or death in patients receiving sotrovimab (6/528; 1%) compared with placebo (30/529; 6%)[3]
- Sotrovimab (500 mg IV) received an Emergency Use Authorization (EUA) in the US for the treatment of mild-to-moderate COVID-19 for patients aged ≥12 years at high-risk for severe disease[4]
- New SARS-CoV-2 variants of concern (VOC) have since emerged. Based on *in vitro* studies against Omicron BA.2, FDA deauthorized sotrovimab in the US starting in late March 2022[2,5-7]
- Sotrovimab 500 mg IV holds current marketing authorization in Europe and current provisional, temporary, or conditional marketing authorization in many countries, including the United Kingdom, Japan, and Australia[8-11]
- Given the lack of data on how *in vitro* antibody neutralization activity for a dual-action antibody translates to clinical effectiveness, we conducted a real-world analysis of COVID-19 patients who were at high-risk of disease progression to estimate the risk of 30-day hospitalization and/or mortality in a large, nationally representative US insurance claims database from September 2021 to April 2022 during the time period when Delta and early Omicron variants were predominant

Objectives

- Describe the demographics and clinical characteristics of patients with claimed diagnosis of COVID-19 treated with sotrovimab and not treated with a mAb
- Analyze the real-world clinical effectiveness of sotrovimab in reducing the risk of 30-day all-cause hospitalization and/or mortality among the overall treated cohort and among high-risk subgroups

Methods

- Study design: Retrospective analysis of de-identified patients diagnosed with COVID-19 (ICD-10: U07.1) in the FAIR Health National Private Insurance Claims (FH NPIC®) database
- Time period: Reported diagnosis of COVID-19 between September 1, 2021 and April 30, 2022
- Patients meeting EUA high-risk criteria were identified via pre-specified ICD-10-CM diagnoses in records ≤24 months prior to their first claimed COVID-19 diagnosis
  - EUA high-risk criteria: age ≥65 years, body mass index ≥25 kg/m^2, pregnancy, chronic kidney disease, type 1 or 2 diabetes, immunocompromising conditions, immunosuppressive therapy, COPD, asthma, chronic lung disease, sickle cell disease, congenital heart disease, acquired heart disease, cardiovascular disease, hypertension, neurodevelopmental disorders and medical device
- Patients were divided into two cohorts based on claimed HCPCS codes for mAb administration: High-risk sotrovimab and High-risk no mAb
- Outcomes:
  - 30-day all-cause hospitalization
  - 30-day facility-reported all-cause mortality (“FR mortality”)
  - 30-day all-cause hospitalization or FR mortality (composite outcome)
- Multivariate Poisson regression analyses were conducted to assess the impact of sotrovimab (vs no mAb) on 30-day hospitalization and/or FR mortality, adjusting for potential confounders
- Propensity score (PS)-matched Poisson regression analyses were also conducted to assess sotrovimab effectiveness among PS-matched cohorts; 15,633 sotrovimab-treated patients were matched with 62,532 no mAb patients (1:4) on diagnosis month, age, gender, region, rurality, and selected high-risk conditions

Results

- The sotrovimab cohort was older and had a greater proportion of patients across the majority of high-risk conditions compared to the no mAb cohort (**Table 1**)
- After adjusting for potential confounders (**Table 2**), compared to no mAb treatment, sotrovimab treatment of high-risk COVID-19 patients diagnosed between September 1, 2021 and April 30, 2022 was associated with:
  - 55% relative risk reduction of 30-day hospitalization or FR mortality
  - 85% relative risk reduction of 30-day FR mortality
- From September 2021 to March 2022, statistically significant adjusted relative risk reductions in 30-day hospitalization or FR mortality ranging from 51% to 71% (PS-matched relative risk reduction of 55% to 73%) (**Table 3**)
- In April 2022, non-significant 46% adjusted relative risk reduction in 30-day hospitalization or FR mortality (68% PS-matched relative risk reduction) due to small sample size (n=68) of sotrovimab-treated patients (**Table 3**)
- Sotrovimab effectiveness persisted across all high-risk subgroups assessed (**Figure 1**)

Table 1: Demographic and Clinical Characteristics by Treatment Cohort

Cohort Characteristics		High-risk Sotrovimab N=15,633		High-risk No mAb[a] N=1,514,868	
		n	%	n	%
Diagnosis Month Category[b]	Sep 1, 2021 – Nov 30, 2021	2,143	13.71	511,292	33.75
	Dec 1, 2021 – Feb 28, 2022	12,376	79.17	820,817	54.18
	Mar 1, 2022 – Apr 30, 2022	1,114	7.13	182,759	12.06
Region[b]	1 & 2	5,450	34.86	516,964	34.13
	3 & 4	3,336	21.34	324,250	21.40
	5 & 7	3,277	20.96	205,595	13.57
	6 & 8	2,055	13.15	271,037	17.89
	9 & 10	1,506	9.63	197,022	13.01
Rurality	Rural	2,847	18.21	208,637	13.77
	Urban	12,786	81.79	1,306,231	86.23
Gender	Female	9,188	58.77	855,221	56.46
	Male	6,445	41.23	659,647	43.54
Age (years)	0-17	87	0.56	117,021	7.72
	18-34	1,909	12.21	279,322	18.44
	35-49	3,815	24.40	411,711	27.18
	50-64	6,627	42.39	512,330	33.82
	65-74	2,348	15.02	131,456	8.68
	75+	847	5.42	63,028	4.16
	Mean (SD)	52.98 (14.53)		45.90 (18.05)	
	Median (IQR)	55.00 (20)		48.00 (25)	

Table 1 (Continued)

Cohort Characteristics		High-risk Sotrovimab N=15,633		High-risk No mAb[a] N=1,514,868	
		n	%	n	%
Documented COVID-19 Vaccine[c]	Yes	3,177	20.32	229,770	15.17
	No/Unknown	12,456	79.68	1,285,098	84.83
High-risk Conditions (EUA)	Obesity (BMI ≥30 kg/m^2)	4,335	27.73	379,463	25.05
	Pregnant	1,203	7.70	75,133	4.96
	Chronic Kidney Disease (CKD)	1,571	10.05	68,168	4.50
	Diabetes	4,081	26.11	268,798	17.74
	Immunocompromising Condition/Immunosuppressive Therapy	6,525	41.74	379,002	25.02
	COPD	1,105	7.07	63,497	4.19
	Asthma	709	4.54	45,930	3.03
	Chronic Lung Disease	2,509	16.05	193,149	12.75
	Sickle Cell Disease	22	0.14	3,727	0.25
	Congenital Heart Disease	265	1.70	23,741	1.57
	Acquired Heart Disease	5,135	32.85	323,485	21.35
	Cardiovascular Disease	4,118	26.34	227,764	15.04
	Hypertension	8,319	53.21	627,283	41.41
	Neurodevelopmental Disorder	970	6.20	188,172	12.42
	Medical Device	1,462	9.35	110,341	7.28

[a]Includes 131 patients identified based on history of drug-induced anaphylaxis, which is not an EUA high-risk condition.
[b]Diagnosis month category reflects the time period for when a circulating variant was or became predominant based on CDC COVID Data Tracker Nowcast; patient-level sequencing data are not available.
[c]The FH NPIC® database included only COVID-19 vaccinations with claims submitted to a contributing insurer. Those without a documented COVID-19 vaccine were of uncertain vaccination status as they could be unvaccinated or vaccinated without a submitted claim to a contributing insurer.

Table 2: Adjusted and Propensity Score–matched Relative Risk of 30-day All-cause Hospitalization or FR Mortality

Outcome	High-risk Sotrovimab N=15,633	High-risk No mAb N=1,514,868	Adjusted RR[a,b] (95% CI)	PS-matched RR[a,c] (95% CI)	*p*-value[d]
30-day Hospitalization	418 (2.67%)	84,307 (5.57%)	0.45 (0.41, 0.49)	0.39 (0.36, 0.43)	<0.0001
30-day FR Mortality	13 (0.08%)	8,167 (0.54%)	0.15 (0.08, 0.29)	0.12 (0.06, 0.24)	<0.0001
30-day Hospitalization or FR Mortality	419 (2.68%)	84,720 (5.59%)	0.45 (0.41, 0.49)	0.39 (0.35, 0.43)	<0.0001

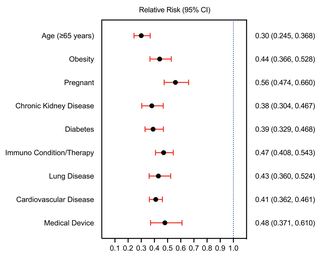
[a]Reference group = high-risk no mAb. [b]Adjusted for diagnosis month category, age, gender, region, rurality, high-risk conditions, and documented COVID-19 vaccine. [c]Matched on diagnosis month, age, gender, region, rurality, and selected high-risk conditions. [d]*p*-value applies to adjusted RR and PS-matched RR.

Table 3: Adjusted and Propensity Score–matched Relative Risk of 30-day All-cause Hospitalization or FR Mortality by Diagnosis Month

Diagnosis Month	High-risk Sotrovimab		High-risk No mAb		Adjusted RR[b,c] (95% CI)	PS-matched RR[c,d] (95% CI)	*p*-value[e]
	N	%[a]	N	%[a]			
Sep 2021	460	4.78	307,096	9.53	0.48 (0.32, 0.72)	0.39 (0.26, 0.60)	0.0002
Oct 2021	451	2.66	84,367	8.62	0.29 (0.17, 0.51)	0.27 (0.15, 0.47)	<0.0001
Nov 2021	1,232	2.76	119,829	7.81	0.33 (0.23, 0.45)	0.32 (0.22, 0.45)	<0.0001
Dec 2021	5,188	3.14	455,706	3.90	0.49 (0.43, 0.57)	0.45 (0.39, 0.53)	<0.0001
Jan 2022	4,859	1.85	261,765	3.37	0.36 (0.30, 0.44)	0.36 (0.29, 0.44)	<0.0001
Feb 2022	2,329	3.26	103,346	6.90	0.43 (0.34, 0.54)	0.40 (0.32, 0.50)	<0.0001
Mar 2022	1,046	2.01	65,521	4.37	0.41 (0.27, 0.62)	0.36 (0.23, 0.56)	<0.0001
Apr 2022	68	1.47	117,238	1.90	0.54 (0.08, 3.54)	0.32 (0.04, 2.38)	0.5185

[a]The reported % = number hospitalized or died in diagnosis month in treatment cohort/number in diagnosis month in treatment cohort. [b]Reference group = high-risk no mAb. [c]Adjusted for diagnosis month category, age, gender, region, rurality, high-risk conditions, and documented COVID-19 vaccine.
[d]Matched on diagnosis month, age, gender, region, rurality, and selected high-risk conditions. [e]*p*-value applies to adjusted RR and PS-matched RR.

Figure 1: Adjusted Relative Risk for the High-risk Sotrovimab-treated Cohort Versus the No mAb Cohort



Note: *p*-value <0.0001 for all high-risk conditions.

Limitations

- Given that sotrovimab had been deauthorized across the entire US on April 5, 2022, the small sample size, together with mixed variant prevalence and lack of specific sequencing data, limits our ability to draw conclusions about sotrovimab effectiveness in April 2022
- Database limited in capturing unbilled services (e.g. vaccinations) and oral drugs billed using National Drug Codes (NDC)
- Facility-reported all-cause mortality likely underestimates death
- Residual confounding due to absence of race/ethnicity information and variant sequencing data

Sotrovimab demonstrated real-world clinical effectiveness during the Delta and early Omicron waves in the US

- Compared to no mAb treatment, sotrovimab treatment was associated with reduced risk of 30-day hospitalization or FR mortality among high-risk patients diagnosed with COVID-19 between September 2021 and April 2022, during the Delta and early Omicron waves in the US
- Sotrovimab clinical effectiveness persisted among all high-risk subgroups assessed

Disclosures

This study is sponsored by Vir Biotechnology in collaboration with GSK. **MMC, SS, CR** are employees of and shareholders of Vir Biotechnology; **DCG, HB, VP, CFB, MD** are employees of and shareholders of GSK.

Acknowledgments

Vir Biotechnology: Anvar Suyundikov, Xiao Ding, M. Cyrus Maher, Wendy Yeh, Amalio Telenti, Tamara Palagashvili, Don Hoang, Wenjie Wang, Hong Wang, Rajendra Joshi, and Yimeng Lu; Fred Hutchinson Cancer Research Center & University of Washington: Lawrence Corey; FAIR Health: Ali Russo, Alexander Mizenko, and Randi Scott for data extraction and statistical analyses. Research based upon data compiled and maintained by FAIR Health, Inc., which is not responsible for the conduct of the research or any of the opinions expressed herein. Editorial assistance was provided by Lumanity Scientific Inc. and was funded by Vir Biotechnology.

Presented at IDWeek; October 19-23, 2022; Washington, DC.

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