Implementation and patient outcomes of a pediatric COVID-19 monoclonal antibody program

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Summary:
This report describes the implementation of a COVID-19 monoclonal antibody referral process and the clinical outcomes of 182 patients who received a SARS-CoV-2 neutralizing monoclonal antibody infusion at a pediatric hospital.

Abbreviations:
ARDS: Acute Respiratory Distress Syndrome
COVID-19: Coronavirus disease 2019
ED: Emergency Department
EMR: Electronic Medical Record
EUA: Emergency Use Authorization
FDA: Food and Drug Administration
GI: Gastrointestinal
ID: Infectious Disease
IRB: Institutional Review Board
mAb: Monoclonal Antibody
NCH: Nationwide Children's Hospital
PDC: Physician Direct Connect
PEP: Post-Exposure Prophylaxis

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Background

The severity and reach of the COVID-19 pandemic drove the development of various therapeutic approaches to combat SARS-CoV-2, including several neutralizing monoclonal antibody (mAb) therapies. A January 2021 pediatric consensus statement opposed routine use and recommended individualized risk assessments when considering COVID-19 mAb therapies in children and adolescents due to limited data. This report describes the implementation of a mAb referral process and clinical outcomes of patients who received a mAb infusion in a pediatric hospital.

Methods

We developed a tiered allocation system based on underlying medical conditions and incorporated it into a standardized COVID-19 mAb referral and approval process. Demographics and clinical data were collected on all patients who received mAb therapy for treatment or post-exposure prophylaxis. Data recorded included socio-demographics, qualifying underlying medical condition, clinical manifestations of infection, and overall course of treatment and disease.

Results

A total of 182 patients ≤21 years old received a COVID-19 mAb infusion between November 27, 2020, and January 26, 2022. Patient age ranged from 10 months to 21 years, with a median age of 15 years. In total, 7 patients (4%) had suspected adverse reactions during the infusion, and 15 (8%) patients required a COVID-19-related visit within 30 days of the mAb infusion.

Conclusion

A tiered allocation process may provide the framework for the stratification and efficient distribution of mAb therapies. Future research must focus on efficacy of these therapies in the pediatric population, standardized therapeutic prioritization, and the optimal timeframe for mAb delivery to prevent progression to severe disease.

Key Words:
COVID-19
Bamlanivimab
Casirivimab
SARS-CoV-2 Neutralizing Antibody
Sotrovimab
Pediatric

Introduction

As of September 2022, over 14 million cumulative cases of COVID-19 were reported in the United States in children under the age of 18 years since the onset of the pandemic.[1] While only a small portion of the total reported cases, some pediatric patients are at risk for progressing to severe disease, hospitalization or death.[2,3] The severity and reach of the COVID-19 pandemic drove the development of various therapeutic approaches to combat SARS-CoV-2, including several neutralizing monoclonal antibody (mAb) therapies.[4-7] However, the lack of initial data resulted in a January 2021 pediatric consensus statement opposing routine use and recommending individualized risk assessments when considering COVID-19 mAb therapies in children and adolescents.[8]

After careful consideration of these recommendations, our institution chose to offer COVID-19 mAb therapies to select patients whose underlying medical condition suggested a favorable risk-benefit ratio. To define appropriate SARS-CoV-2 mAb use in children and adolescents, we developed a tiered allocation system based on underlying medical condition and incorporated it into a standardized COVID-19 mAb referral and approval process. The purpose of the combination tiered allocation and referral system was to support distribution of a scarce resource in pediatric patients, provide clear guidance on risk stratification, and offer subspecialists and community practitioners a streamlined approach to treating patients at greatest risk for severe disease. Here we present a descriptive report on patients who received a SARS-CoV-2 neutralizing mAb therapy through a COVID-19 mAb allocation and referral process at a pediatric hospital.

Methods

Nationwide Children's Hospital (NCH) is a free-standing children's hospital with 527 licensed beds located adjacent to downtown Columbus, Ohio. The downtown campus has an emergency department (ED), urgent care center, and primary care clinic. In addition, off-

campus locations include a second ED, 6 additional urgent care centers, and 12 additional primary care clinics scattered around the metropolitan area. NCH is the only children's hospital in Columbus, with a wide catchment area in central and southeast Ohio. Approximately 1.6 million outpatient visits and 20,000 inpatient discharges occur annually.

Development of a COVID-19 Monoclonal Antibody Process.

COVID-19 mAb therapy became available for patients at NCH in November 2020. Due to the limited supply and uncertain demand, our team developed a tiered eligibility and referral process to target pediatric patients at highest risk for developing severe COVID-19. In addition to mAb supply concerns, limited staff and physical space to dedicate to mAb administration was a substantial challenge, particularly since the patients (at least initially, prior to authorization of post-exposure prophylaxis [PEP]) were infected with SARS-CoV-2 and required airborne isolation. At the time of initial planning, we also discussed the process with NCH's COVID-19 Scarce Resource Committee—a group developed by hospital leadership to ensure equitable distribution of scarce resources during the pandemic. Two authors served on this committee (J.E.B., J.R.W.).

Referral Process.

Referrals for mAb therapy were accepted through NCH's Physician Direct Connect (PDC) service, a call line for referring clinicians to connect with NCH specialists for telephone consultation. PDC existed prior to the COVID-19 pandemic and is available to both NCH and external providers 24 hours per day, 7 days per week. Clinicians calling for mAb therapy were connected with the attending infectious diseases (ID) physician on call. The ID physician reviewed eligibility criteria, including age/weight, duration of symptoms (or, for PEP, date of exposure), presence of a qualifying high-risk condition (see explanation of tier system below), and positive viral test result. For most of the study time period, we required a documented positive viral test, meaning an antigen or nucleic acid test performed

in a healthcare setting or a proctored rapid home test. However, in January 2022, when proctored home tests were no longer widely available during the omicron surge, we accepted any positive home test. Once the ID physician approved mAb therapy, the patient was scheduled for an appointment. Our goal was to schedule the infusion within 2 days of the referral; however, during times when referral volume surged, this was not always possible. For two patients who did not meet the Emergency Use Authorization (EUA) age and weight criteria for treatment, compassionate use authorization was obtained from the Food and Drug Administration (FDA).

Administration Process.

After considering various spaces in off-site areas or building a temporary location within the hospital system, we decided to provide mAb therapy on main campus due to its central location and overall accessibility for all potential patients. From November 2020 through December 2021, most patients scheduled for mAb therapy were admitted to the hospital as an "outpatient in a bed" on our 26-bed ID inpatient unit. Due to room (in particular, airborne isolation rooms) and nursing availability constraints, we offered 2 infusions per day Monday through Friday, and 1 infusion each day on weekends and holidays. Patients hospitalized on other units for reasons other than COVID-19, but who met criteria for mAb therapy, received mAb on their respective inpatient units after approval by ID. Some Hematology/Oncology patients were also treated in the Hematology/Oncology outpatient infusion clinic.

On the ID unit, inpatient medical teams reviewed EUA information with patients/caregivers, provided the required fact sheet, obtained verbal consent, and documented in the medical record. Nurses administering mAb therapy were limited to a single patient initially, but once the staff became accustomed to providing mAb infusions, they carried a typical patient load of 3-4 patients. Patient monitoring included vital signs prior

to infusion, every 15 minutes during the infusion, and 60 minutes after the infusion completed. In October 2021, we secured a team of nurse practitioners to manage the mAb infusion process, including all aspects of EUA requirements, verbal consent, orders, nursing care, discharge education, and documentation. In January 2022, we set up a "COVID-19 monoclonal antibody clinic" that utilized four rooms in the ED, completely managed by the nurse practitioner team. With the move, we were able to provide up to 4 infusions per day, Monday through Saturday.

Development of High-Risk Condition Tiers.

With the goal of administering mAb therapy to patients at the greatest risk for progression to severe COVID-19, we developed tiers that risk-stratified underlying conditions. The tiers were based on high-risk conditions specified in the EUA fact sheets,[9,10] conditions highlighted by the Centers for Disease Control and Prevention,[11] guidelines from the National Institutes of Health,[12] published literature addressing risk factors in children,[2,13-17] review of local hospitalization data, and local expert opinion (Supplemental Material). As new information became available, we modified the tiers accordingly. The most recent version of our tier system is shown in Table 1. As case numbers and drug supply fluctuated, we narrowed or broadened which tiers were eligible for therapy (e.g., currently we offer to all tiers 1-3). PEP was incorporated into our tier system August to December 2021, when products authorized for PEP were active against circulating variants. At no time did vaccination status impact which patients were offered mAb therapy.

Retrospective Data Collection

All patients aged ≤21 years who received mAb therapy for treatment or PEP of SARS-CoV-2 from November 2020 through January 2022 were included in the data analysis. Four monoclonal antibody therapies were authorized and available during this period: Bamlanivimab (Eli Lilly and Company), November 2020 – February 2021;

Casirivimab/Imdevimab (Regeneron Pharmaceuticals, Inc.), March 2021 – December 2021; Bamlanivimab/Etesevimab (Eli Lilly and Company), March 2021 – April 2021 and September 2021 – December 2021; and Sotrovimab (GlaxoSmithKline and Vir Biotechnology), December 2021 – January 2022. Institutional Review Board approval was obtained for data collection within the electronic medical record. The information recorded included socio-demographics, qualifying underlying medical condition, clinical manifestations of infection, and overall course of the treatment and disease.

Socio-demographic data comprised age, race, and gender, with race further defined as White, Black, Asian, and Other. All qualifying underlying medical conditions were recorded from the electronic medical record. Clinical manifestations of infection were defined as symptoms present at infusion. Additional clinical data to define the course of infection included the following: dates of positive SARS-CoV-2 viral test and symptom onset; date and name of mAb therapy received; COVID-19 vaccination status; any symptoms or adverse drug reactions noted during the mAb infusion; and outcomes of COVID-related healthcare visits 30-days post infusion. A tier status was defined for each patient based on the qualifying comorbidities at the time of infusion in relation to tiers in Table 1.

Results

A total of 182 patients aged ≤21 years received neutralizing COVID mAb therapy at NCH between November 27, 2020, and January 26, 2022 (Table 2). Of these, 171 patients presented for symptomatic treatment and 11 patients for PEP. Patient age ranged from 10 months to 21 years, with a median age of 15 years. In total, 140 (77%) patients were under the age of 18 years, with 79 (43%) between the ages of 12-15 years and 48 (26%) between 16-17 years. Male and female sex were equally represented.

Most patients receiving a mAb infusion were designated Tier 1. Therefore, severe obesity, severe immunosuppression, or medical complexity were the top qualifying

underlying medical conditions at infusion. Overall, 7 patients (4%) had suspected adverse reactions at infusion. Reported symptoms included: an elevated blood pressure; nausea and a local infusion site reaction; mild bradycardia; two cases of chest tightness; tremors; and a self-reported "itchy mouth" in one patient. Two patients received treatment with diphenhydramine and two received a decrease in the infusion rate, however all patients completed therapy. No patients required follow-up care related to adverse drug reactions post-infusion.

In the subset of patients (15; 9%) who required a COVID-19-related medical encounter within 30 days post-infusion (Table 3), the average timeframe from symptom onset to infusion was 4 days. Two of these COVID-19-related post-infusion encounters were telephone call consultations for treatment-emergent adverse effects or ongoing COVID-19 symptom management. Thirteen patients required a medically attended post-infusion COVID-19 visit. Two patients were seen post-infusion by their primary care provider, while three patients received care in the ED and eight patients were hospitalized. One hospitalized patient progressed to requiring remdesivir therapy one day post-infusion and one patient with severe immunosuppression undergoing active chemotherapy treatment expired from COVID-19-related complications 23 days post infusion. Both patients received a COVID-19 mAb infusion within 1 day of a positive test, but self-reported symptom onset 6 days prior to the infusion.

Children less than 12 years old

Bamlanivimab/etesevimab was briefly available for pediatric patients less than 12 years of age in the fall of 2021 (Table 4). Nine patients under the age of 12 years with SARS-CoV-2 infection received bamlanivimab/etesevimab for treatment while 2 additional patients received the therapy as PEP. Casirivimab/imdevimab infusions were administered in 2 patients as treatment for SARS-CoV-2 infection via compassionate use approval from the

FDA. All infusions in pediatric patients less than 12 years were well tolerated, and no adverse events were reported. Of the 11 patients who received mAb treatment, the time from symptom onset to infusion ranged from less than 1 day to 7 days (median: 3 days). One patient required additional COVID-19-related follow-up care twice within 30 days following the mAb infusion.

Discussion

Our referral and allocation program faced several challenges, including a sporadic mAb supply chain and evolving variants with unique susceptibility, that had to be carefully balanced with limited pediatric mAb data. The Department of Health and Human Services reversed a decision to allow direct ordering of mAb products by hospitals in September 2021 due to a substantial surge of the Delta variant. Distribution of mAb therapies was delegated to state health departments, with overall state allocations—and thus local allocations—dependent on weekly COVID-19 cases and mAb usage reported to federal databases.[18] Frequent communication between our pharmacy, who completed the weekly allocation surveys, and the ID teams was vital to the success of our program to ensure an adequate supply was available for scheduled mAb infusion appointments.

The use of any individual or combination mAb therapy at our hospital was driven by institutional restrictions and variant susceptibility to the product within our region. When multiple mAb products were available, our hospital chose to limit provider access within the EMR to a single therapy in order to reserve novel mAbs for future variants. During our reporting period, evidence of marked reduction in susceptibility to bamlanivimab/etesevimab was noted for beta (B.1.351) and gamma (P.1) SARS-CoV-2 variants, while sotrovimab remained the only mAb demonstrating activity to the omicron (B.1.1.529) variant.[12] Our tiered allocation system and EMR restrictions allowed our team to quickly transition between mAb products and limit patient approvals to the highest-risk conditions (e.g. Tier 1) when

supply chain or variant susceptibility was in question.

Data on the safety and efficacy of COVID-19 mAb therapy continues to emerge, but pediatric data remains scarce.[19] In comparison to published adult studies, our data suggests a higher incidence of COVID-19 related care post-mAb administration, but a lower incidence of adverse drug events in the pediatric population. [20-22] It is plausible that our tiered allocation structure limited our data pool to higher acuity patients who were predisposed to a higher likelihood of post-infusion COVID-19 related care. We also chose a broad interpretation of COVID-19 symptom relation; if a self-reported symptom at infusion resulted in a post-infusion care, it was included in our data set. While routine use in any pediatric patient with a qualifying risk factor is not recommended by national consensus documents, COVID-19 mAb therapy should be considered for adolescents at highest risk of severe disease to prevent progression.[23] Future revisions to our tiered allocation system must continue to review outcomes of high-risk pediatric patients while assessing the overall place of mAbs in therapy in relation to other antiviral treatments.

Our report has several limitations. First, because of the retrospective design, the clinical manifestations of COVID-19 reflect self-reported symptoms at the time of the infusion and may not include all symptoms present over the course of the infection. In addition, the adverse events and outcomes within this single-arm design may not be equivalent to those of a randomized, controlled trial. Second, it is possible that we missed some post-infusion COVID-19-related visits if patients presented to a non-NCH facility. Third, the safety data and overall process is reflective of a pre-omicron cohort and may not be generalizable currently to pediatric hospitals; therefore it is unclear if this data could impact the practice at other institutions. Finally, it is important to recognize that we included some adult patients, ages 18-21, who are managed by pediatric subspecialists at NCH. Thus, our

data are not purely pediatric but nonetheless are representative of many pediatric hospitals who manage cohorts of patients into adulthood.

Conclusion

Overall, the implementation of a COVID-19 mAb therapy program utilizing a 24-hour per day, 7-day per week referral process, an accessible location, and tiered allocation criteria for approval was successful in providing timely access to mAb therapy, efficiently incorporating the emergence of new COVID-19 risk stratification data and managing a limited drug supply. Limitations to physical space and nursing staff were substantial challenges in the process and were largely alleviated by creating a dedicated infusion clinic space in unused ED rooms staffed by nurse practitioners. Our process may provide a framework for institutions developing a mAb program in high-risk COVID-19 pediatric patients. Further work is necessary to reduce barriers to COVID-19 treatments and increase knowledge of available therapies. It should be noted that new COVID-19 therapeutic options, including oral antivirals and outpatient intravenous remedesivir, may better address the physical, medical, and ethical barriers. Future research must focus on efficacy and outcomes of all these therapies in the pediatric population, standardized prioritization based on underlying medical conditions, and the optimal timeframe for therapeutic delivery for the most at-risk patients to prevent progression to severe disease.

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Table 1: COVID Monoclonal Antibody Pediatric Allocation Tiers

Tier	EUA Qualifying Higher-Risk Underlying Medical Condition	Definition
1	Severe obesity	Body Mass Index ≥35 kg/m^2 or ≥120% of the 95th percentile for age
	Neurodevelopmental, genetic, or metabolic disorder conferring medical complexity	For example, cerebral palsy, Trisomy 21
	Dependence on respiratory technology	Tracheostomy or positive pressure ventilation not related to COVID-19
	Severe immunosuppression	At least one of the following: • Undergoing treatment for cancer • Solid organ transplant within the past 3 months or any history of lung transplant • Bone marrow transplant within the past 12 months or receiving immunosuppressive therapies • Primary immunodeficiency disorder with profound T or B cell dysfunction • T-cell depleting therapy with CD4 count <300 cells/mm^3 or, for children, <15% • B-cell depleting therapy within the past 6 months and no evidence of B cell recovery • Hypogammaglobulinemia <500 • Systemic corticosteroids with prednisone equivalent of ≥20 mg/day or ≥2 mg/kg/day for ≥ 14 days • Advanced or untreated HIV • Other immunocompromised host with absolute lymphocyte count <300 cells/mm3
2	Higher-Risk Cardiac Disease	At least one of the following: • Uncorrected or palliated cyanotic congenital heart disease • Hemodynamically significant congenital heart disease (as determined by Cardiologist) • One pumping chamber • Heart failure • Significant pulmonary hypertension requiring vasodilatory therapy
	Higher-Risk Pulmonary Disease	Chronic respiratory or neuromuscular condition accompanied by at least one of the following: • Severe obstructive or restrictive disease (as determined by Pulmonologist) • Chronic oxygen requirement • Interstitial lung disease dependent on oxygen or systemic steroids
	Type 1 Diabetes Mellitus (regardless of control)	
	Obesity in addition to at least one modified higher-risk EUA criterion	Body Mass Index ≥30 kg/m^2 or ≥95th percentile for age
3	Any modified high-risk EUA criterion	At least one of the following: • Age ≥65 years • Obesity (Body Mass Index ≥30 kg/m^2 or ≥95th percentile for age) • Pregnancy

		• Chronic kidney disease • Chronic liver disease • Diabetes (Type 1 or 2) • Immunosuppressive disease or immunosuppressive treatment • Cardiovascular disease (including congenital heart disease) or hypertension • Chronic lung diseases (including severe asthma but not mild-moderate asthma) • Sickle cell disease • Neurodevelopmental disorders or other conditions that confer medical complexity • Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID 19))

EUA, emergency use authorization

Table 2: Characteristics and clinical outcomes of 182 patients receiving a COVID-19 monoclonal antibody at a pediatric hospital

	Overall *n= 182*	**Bamlanivimab or Bamlanivimab/ Etesevimab** *n=38 (21%)*	**Casirivimab / Imdevimab** *n = 96 (53%)*	**Sotrovimab** *n=48 (26%)*
Dates of Use	11/27/2020 - 1/26/2022	11/27/2020 - 12/29/2021	3/16/2021 - 12/23/2021	12/27/2021 - 1/26/2022
Age (years)				
Median [Min, Max]	15 [0.8,21]	13 [0.8,21]	16 [5,21]	16 [12,20]
0 - 4	2 (1%)	2	0	0
5 - 11	11 (6%)	9	2	0
12 - 15	79 (43%)	15	45	19
16 - 17	48 (26%)	7	25	16
18 - 21	42 (23%)	5	24	13
Gender				
Male	96 (53%)	18	49	29
Female	86 (47%)	20	47	19
Race *(as documented in medical record)*				
White	117 (64%)	29	55	32
Black	39 (21%)	6	27	6
Asian	4 (2%)	1	3	0
Other	22 (12%)	2	10	10
Not Reported	1 (1%)	0	1	0
Underlying Medical Condition				
Severe Obesity	64 (35%)	6	36	22
Severe Immunosuppression	45 (25%)	10	23	12
s/p Solid Organ Transplant	*0*	*0*	*0*	*0*
Immunosuppressive Disorder or Therapy	*29*	*7*	*15*	*7*
Active Hematology/Oncology Disorder	*16*	*3*	*8*	*5*
Medically Complex	29 (16%)	8	9	12
Obesity	15 (8%)	1	13	1
Type 1 Diabetes	15 (8%)	3	7	5
Dependence on Respiratory Technology	7 (4%)	2	2	3

Higher-Risk Cardiac Disease	4 (2%)	0	3	1
Higher-Risk Respiratory Disease	4 (2%)	0	2	0
Tier Classification				
1	124 (68%)	22	58	44
2	22 (12%)	4	15	3
3	36 (20%)	12	23	1
Onset of Symptoms to Infusion (Days)*				
Median [Min, Max]	4 [<1, 10]	4 [<1,7]	4 [<1,9]	6 [1,10]
Self-reported Symptoms at Time of Infusion*				
Cough	116 (64%)	18	63	35
Congestion	62 (34%)	8	36	18
Sore Throat	53 (29%)	9	27	17
Fever	51 (28%)	16	29	6
Fatigue	51 (28%)	12	34	5
Rhinorrhea	46 (25%)	9	24	13
Headache	41 (23%)	6	29	6
Myalgia/Body Ache	33 (18%)	6	26	1
Dyspnea/Chest Pain	28 (15%)	6	18	4
Diarrhea	19 (10%)	5	11	3
Nausea/Vomiting	17 (9%)	3	12	2
Loss of taste/smell	16 (9%)	2	10	4
Abdominal Pain	13 (7%)	2	10	1
Rash	6 (3%)	2	3	1
Positive COVID-19 Test to Infusion (Days)*				
Median [Min, Max]	2 [<1,10]	2 [<1,7]	2 [<1,8]	3 [1,10]
Suspected Adverse Drug Reactions				
Yes	7 (4%)	4	3	0
No	175 (96%)	34	93	48
30-days post-infusion COVID-19-related visits				
Yes	15 (8%)	3 (8%)	9 (9%)	3 (6%)
No	167 (92%)	35	87	45

**Data does not include patients receiving prophylactic therapy*

Table 3: Characteristics and outcomes of patients requiring a COVID-19-related encounter within 30 days of a neutralizing SARS-CoV-2 monoclonal antibody infusion

Age	Tier	Qualifying Underlying Medical Condition	Therapy	Onset of Symptoms to Infusion (Days)	Positive Test to Infusion (Days)	COVID-19-related encounters within 30-days post-infusion		Vaccinated at time of infusion?
14	2	Obesity, T1DM	Sotrovimab	3	2	Telephone Consultation	Telephone call concerning rash <1 day post-infusion.	No*
20	3	Sickle Cell	Casirivimab/Imdevimab	5	1	Telephone Consultation	ED telephone triage 9 days post-infusion for ongoing nausea and fever. No further progression.	No*
14	3	Chronic Lung Disease	Casirivimab/Imdevimab	7	3	PCP	Primary care visit for continued stomach pain 21 days post infusion.	No*
17	3	Chronic Lung Disease	Bamlanivimab	4	3	PCP	Primary care consultation for continued shortness of breath 7 days post-infusion.	No*
14	3	Chronic Lung Disease	Bamlanivimab	1	1	ED	Presented to ED 3 days post infusion for ongoing COVID-19 symptoms; discharged home.	Not eligible
14	1	Severe Obesity	Casirivimab/Imdevimab	4	4	ED	Presented to ED 9 days post-infusion for bilateral leg pain and shortness of breath; discharged home.	Fully Vaccinated (5.5 months prior)
19	1	Medical Complexity	Sotrovimab	7	5	ED	Presented to ED 2 days post-infusion for shortness of breath and chest tightness; discharged home.	No*
10 mos.	1	Medical Complexity	Bamlanivimab/Etesevimab	1	1	Inpatient Admission	Hospitalized for respiratory distress 12 days post-infusion; discharged home. Hospitalized 14 days post-infusion for gastrointestinal concerns.	Not eligible
5	1	Severe Immunosuppression	Casirivimab/Imdevimab	3	2	Inpatient Admission	Hospitalized 1-day post-infusion due to multiple infections (COVID-19, norovirus, *Clostridioides difficile*)	Not eligible
15	3	Immunosuppressive Treatment	Casirivimab/Imdevimab	5	1	Inpatient Admission	Hospitalized 18 days post infusion for pain and fever of unknown etiology. Initial symptoms of COVID-19 improved.	No*
16	1	Severe Immunosuppression	Casirivimab/Imdevimab	6	<1	Inpatient Admission	Hospitalized 9 days post-infusion for nephrolithiasis and hydropneumothorax. Patient expired 23 days post-infusion from pulmonary insufficiency due to sarcoma	No*

						exacerbated by COVID-19.	
16	1	Medical Complexity	Sotrovimab	1	1	Inpatient Admission	Hospitalized 6 days post-infusion for respiratory distress and discharged. Readmitted 9 days post-infusion for pneumonia.	No*
17	1	Severe Immunosuppression	Casirivimab/Imdevimab	2	2	Inpatient Admission	Hospitalized 11 days post-infusion for respiratory symptoms and diagnosed with influenza. Discharged home on oseltamivir.	No*
18	1	Medical Complexity	Casirivimab/Imdevimab	2	1	Inpatient Admission	Hospitalized 3 days post-infusion for a urinary tract infection, cellulitis, and COVID-19 pneumonia.	No*
18	1	Severe Immunosuppression	Casirivimab/Imdevimab	6	1	Inpatient Admission	Hospitalized to monitor underlying cardiomyopathy. Progressed to remdesivir therapy 1-day post-infusion.	No*

ARDS, acute respiratory distress syndrome; ED, emergency department; PCP, primary care provider

*Patient self-reported as not vaccinated and/or no record of vaccination in the electronic medical record

Table 4: High-risk patients <12 years of age receiving a COVID-19 monoclonal antibody therapy

Patient	Age	Gender	Race	Qualifying Underlying Medical Condition(s)	Tier	Therapy	Type of Therapy	Symptom Onset to Infusion (Days)	Positive Test to Infusion (Days)	Symptoms at Infusion	Adverse Reaction (Yes/No)	COVID-related visit post infusion (Yes/No)
1	10 mos.	M	White	Medically Complex	1	Bamlanivimab/Etesevimab	Treatment	1	1	Fever, irritability, diarrhea, activity change	No	Yes, presented to ED for respiratory distress 12 days post-infusion. Hospitalized 14 days post-infusion for GI concerns.
2	2	F	White	Medically Complex	1	Bamlanivimab/Etesevimab	Treatment	5	2	Rhinorrhea, diarrhea, fever	No	No
3	5	F	White	Severe Immunosuppression	1	Bamlanivimab/Etesevimab	Treatment	<1	<1	Rhinorrhea	No	No
4	5	M	Other	Severe Immunosuppression	1	Casirivimab/Imdevimab	Treatment, Compassionate Use*	3	2	Rhinorrhea, cough, fever, irritability, abdominal pain, diarrhea	No	Yes, hospitalized 1-day post-infusion for febrile neutropenia in the setting of multiple infections.
5	5	M	White	Severe Immunosuppression	1	Bamlanivimab/Etesevimab	Post-Exposure Prophlyaxis	n/a	n/a	n/a	No	No
6	9	F	White	Severe immunosuppression	1	Bamlanivimab/Etesevimab	Treatment	<1	<1	None reported	No	No
7	10	F	Other	Severe immunosuppression; dependence on respiratory technology	1	Bamlanivimab/Etesevimab	Post-Exposure Prophlyaxis	n/a	n/a	n/a	No	No
8	10	M	White	Severe immunosuppression; medically complex; higher risk pulmonary disease	1	Bamlanivimab/Etesevimab	Treatment	7	7	Cough, fatigue, fever, headache	No	No
9	10	M	Black	Medically Complex	1	Bamlanivimab/Etesevimab	Treatment	7	2	Cough, rhinorrhea, congestion, fatigue	No	No
10	10	M	Black	Medically Complex	1	Bamlanivimab/Etesevimab	Treatment	5	2	Fever, rhinorrhea, fatigue	No	No
11	11	F	Other	Severe Immunosuppression	1	Bamlanivimab/Etesevimab	Treatment	4	1	Fatigue, fever, congestion, rhinorrhea,	No	No

										cough		
12	11	F	Other	Severe Immunosuppression	1	Casirivimab/Imdevimab	Treatment, Compassionate Use*	2	2	Cough, rhinorrhea	No	No
13	11	M	Black	Type 1 Diabetes Mellitus	2	Bamlanivimab/Etesevimab	Treatment	3	2	Abdominal pain, sore throat, cough, congestion, dizziness	No	No

**Emergency use approval obtained by provider through Food and Drug Administration*