Patient Characteristics

Characteristic	Total N=367
Age – yr	
>75	74 (20)
65-74	98 (27)
55-64	108 (29)
<55	87 (24)
Male sex – no. (%)	201 (55)
Race – no. (%)	
White	276 (75)
Black	54 (15)
Asian	10 (2.7)
Latino/Hispanic	9 (2.4)
Other	7 (1.9)
Unknown	11 (3)
Risk factor for hospitalization – no. (%)	
Age >65y	164 (45)
Age >55y + Hypertension	115 (31)
Immunosuppression	91 (25)
Body-mass index >35	83 (23)
Diabetes mellitus	78 (21)
Age>55y + COPD	67 (18)
Age >55y + CAD	50 (14)
Chronic Kidney Disease	24 (6.5)
>1 Risk factor	232 (63)
Vaccinated for SARS CoV-2 – no. (%)	N=32
1 dose of vaccine	30 (94)
mRNA	28 (88)
JNJ	2 (6)
COVID-19 ³ 10 days from dose	19(59)
2 doses of mRNA vaccine	2 (7)

COVID-19 course

COVID-19 course	Total N=367
Monoclonal Antibody received	
bamlanivimab	190 (52)
casirivimb/Imdevimab	93 (25)
bamlanivimab/etesevimab	84 (23)
Infusion reaction – no. (%)	
Acute	3 (0.8)
Leading to infusion cessation	2 (0.5)
Delayed	1 (0.2)
Time to symptom resolution after infusion – no (%)	N=236
1-2 d	92 (39)
3-5 d	80 (34)
6-11 d	34 (14)
14+ d	30 (13)
Hospitalized for COVID-19 after infusion	
Total – no. (%)	20 (5)
Within 24h of infusion	11 (3)
Within 7d of infusion	8 (2)

Community Need Index and Social Vulnerability Index by Zipcode

Community Need Index, N=352, no. - %	Social Vulnerability Index, N=352, no. - %
5 – 15 (4)	0.9-1 – 13 (4)
4 – 75 (21)	0.7-0.8 – 83 (23)
3 – 91 (26)	0.5-0.6 – 61 (17)
2 – 142 (40)	0.3-0.4 – 77 (22)
1 – 29 (8)	0.1-0.2 – 63 (18)
	0 – 55 (16)
(3.5-5) – 135 (38)	(0.5-1) - 157 (45)
(1-3.5) – 217 (62)	(0-0.5) – 195 (55)

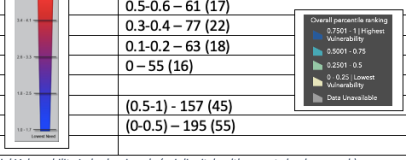

Table 3 Community Need Index and Social Vulnerability Index by zipcode (cni.dignityhealth.org, atsdr.cdc.gov,n.d.)

Conclusion. Our study demonstrates that treatment with anti-SARS-CoV-2 monoclonal antibodies is feasible in a high resource setting. There were no related SARS-CoV-2 exposures and therapy was well tolerated. Trials of anti-SARS-CoV-2 monoclonal antibodies have reported lower rates of hospitalizations in treated patients than we found. This may reflect the expanded time frame for EUA therapy as compared to clinical trials, differences in real world patients or viral variants. Given potential benefit in unvaccinated patients or those at risk for poor vaccine response, the equitable utilization of anti-SARS-CoV-2 monoclonal antibody therapy in early COVID-19 should remain a focus for researchers and clinicians.

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515. Evolution of Treatment Patterns for Patients Hospitalized with COVID-19 in the United States

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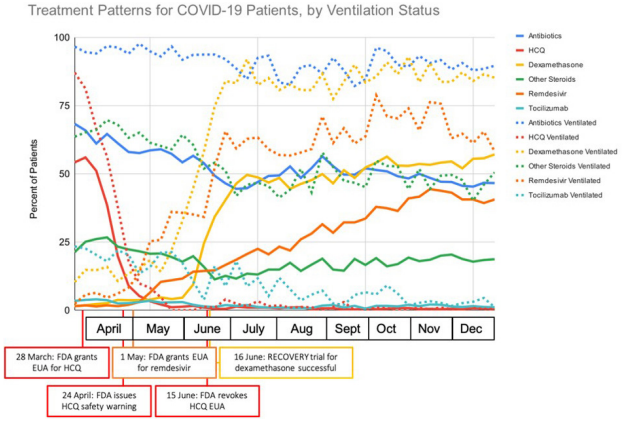
Session: P-24. COVID-19 Treatment

Background. COVID-19 remains a threat to public health, with over 30 million cases in the US alone. As understanding of optimal patient care has improved, treatment guidelines have continued to evolve. This study characterized real-world trends in treatment for US patients hospitalized with COVID-19, stratified by whether patients required invasive ventilation.

Methods. US patients diagnosed and hospitalized with COVID-19 between March 23 and December 31, 2020, in the Optum de-identified COVID-19 electronic health record (EHR) data set were identified. Both drug and procedure codes were used to ascertain medications, and both procedure and diagnostic codes were used to detect invasive ventilation during hospitalization. Medication trends were estimated by computing proportions of hospitalized patients receiving each drug weekly during the study period.

Results. In this cohort of 71,366 hospitalized patients, the largest observed change in care was related to chloroquine/hydroxychloroquine (HCQ) (Figure). HCQ usage peaked at 87% of patients receiving invasive ventilation (54% without ventilation) in the first week of this study (March 23-29), but declined to < 5% of patients, regardless of ventilation status, by the end of May. In contrast, dexamethasone usage was 10% at baseline in patients receiving ventilation (1% without ventilation) and increased to a steady state of >85% of patients receiving ventilation (>50% without ventilation) by the end of June. Similarly, remdesivir usage increased sharply from a baseline of 2% of patients and continued to rise to a peak of 79% of patients receiving invasive ventilation (44% without ventilation) in November before declining.



Conclusion. Meaningful shifts in treatments for US patients hospitalized with COVID-19 were observed from March through December 2020. A dramatic decline was observed for HCQ use, likely owing to safety concerns, while usage of dexamethasone and remdesivir increased as evidence of their efficacy mounted. Across medications, usage was substantially more prevalent among patients requiring invasive ventilation compared with patients with less severe cases.

Disclosures. **Kelly Zalocusky, PhD**, **F. Hoffmann-La Roche Ltd.** (Shareholder)**Genentech, Inc.** (Employee) **Shemra Rizzo, PhD**, **F. Hoffmann-La Roche Ltd.** (Shareholder)**Genentech, Inc.** (Employee) **Devika Chawla, PhD MSPH**,

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516. Evaluation of COVID-19 Monoclonal Antibody Therapies for the Treatment of Non-hospitalized Patients with COVID-19

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Session: P-24. COVID-19 Treatment

Background. In an effort to reduce strain on healthcare systems with patient hospitalizations and deaths due to COVID-19, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for 2 monoclonal antibodies for the treatment of COVID-19 in November 2020: bamlanivimab (BAM) and casirivmab-imdevimab (CAS-IMD). While clinical trial data demonstrated reductions in hospitalization rate, real-world data at the time of approval was vastly limited.

Methods. A retrospective chart review of non-hospitalized patients who received either BAM or CAS-IMD from November 27th, 2020 to February 16th, 2021. Variables included timing of monoclonal antibody infusion, adverse events, and 30-day hospitalization rate. Descriptive statistics were calculated for all data.

Results. 101 patients received either BAM (75.2%) or CAS-IMD (24.8%) at a median of 6 days (IQR 4-7) from reported symptom onset. The most commonly reported symptoms of COVID-19 at time of referral were cough (57.4%), fever (29.7%), and myalgia (27.7%). All patients (100%) had at least 1 documented EUA defined risk factor for severe COVID-19 (Table 1). Following transfusion, 7/101 (6.9%) and 3/101 (3.0%) experienced mild to moderate and severe adverse events, respectively (Table 2). At day 30, 5 patients (5.0%) were hospitalized with COVID-19 at a median of 7 days (IQR 3-8) post monoclonal antibody infusion.

Table. 1 Risk Factors for Severe Disease

Risk Factor	No. (%) (n=101)
BMI ≥ 35 kg.m^2	13 (12.9)
Chronic kidney disease	8 (7.9)
Diabetes	28 (27.7)
Immunosuppressive Disease	41 (40.6)
Acute myeloid leukemia	1 (2.4)
Heart transplant	2 (4.9)
HIV	2 (4.9)
Hematopoietic stem cell transplant	4 (9.8)
Kidney-pancreas transplant	1 (2.4)
Kidney transplant	15 (36.6)
Liver-kidney transplant	1 (2.4)
Liver transplant	14 (13.9)
Lymphocytic lymphoma	1 (2.4)
Receiving Immunosuppressive Treatment	48 (47.5)
≥ 65 years	29 (28.7)
≥ 55 years and cardiovascular disease	5 (5.0)
≥ 55 years and hypertension	9 (8.9)

Table 2. Adverse Events

	No. (%) (N=101)
Mild to moderate	7 (6.9%)
Gastrointestinal upset	2 (28.6)
Elevated blood pressure	1 (1.4)
Chills	2 (28.6)
Headache	2 (28.6)
Severe[a]	3 (3.0)
Systolic blood pressure greater than 200 mmHg	2 (66.6)
Diarrhea and vomiting	1 (33.3)

[a] Serious adverse event defined as an event not present at baseline or was an exacerbation of a preexisting condition occurring during the observation period requiring admission to an evaluation and treatment center

Conclusion. We observed a higher frequency of hospitalization compared to 1.6% for BAM in BLAZE-1 and 3% for CAS-IMD in REGN-COV-2. This observation may reflect our higher risk population as all patients presented with at least 1 risk factor for severe disease compared to 69.6% and 65.0% in BAM and CAS-IMD clinical trials, respectively. Additionally, patients presented with longer durations of symptoms prior to infusion in our study population compared to 3 days reported in BAM and 4 days reported in CAS-IMD trials. Since the conclusion of this study, the FDA revoked the EUA for BAM administered alone based on increased observations of resistant variants to BAM monotherapy. However, our observations highlight the need for further exploration in the prevention of hospitalization in high risk populations as well as the optimal timing of monoclonal antibody therapy.

Disclosures. **All Authors**: No reported disclosures

517. Subcutaneous Sarilumab for the Treatment of Hospitalized patients with Moderate to Severe COVID19 Disease: A Pragmatic, Embedded, Multi-Center Randomized Clinical Trial

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Session: P-24. COVID-19 Treatment

Background. The aim of this pragmatic, embedded adaptive trial was to measure the effectiveness of subcutaneous sarilumab in addition to an evolving standard of care for clinical management of inpatients with moderate to severe COVID-19 disease (NCT04359901). The study is also a real-world demonstration of the realization of a prospective learning healthcare system.

Methods. Two-arm, randomized, open-label controlled 5-center trial comparing standard care alone to standard care (SOC), which evolved over time, with addition of subcutaneous sarilumab (200 mg or 400 mg anti-IL6R) among hospitalized patients with moderate to severe COVID-19 not requiring mechanical ventilation. The primary outcome was 14-day incidence of intubation or death. The trial used a randomized play-the-winner design and was fully embedded within the EHR system, including the adaptive randomization process.

Results. Among 417 patients screened, 162 were eligible based on chart review, 53 consented, and 50 were evaluated for the primary endpoint of intubation or death (>30% of eligible patients enrolled) (Figure 1). After the second interim review, the unblinded Data Monitoring Committee recommended that the study be stopped due to concern for safety: a high probability that rates of intubation or death were higher with addition of sarilumab to SOC (92.6%), and a very low probability (3.4%) that sarilumab would be found to be superior.

Figure 1. Key Study Milestones, Outcomes, and Adaptations

Time	Study Milestone	Sarilumab (Events/Subjects)	Standard of Care (Events/Subjects)
		Randomization Ratio 1:1	
	Study Start Until N=30 Enrolled	5/14	1/15
		First Interim Analysis	
		Probability Sarilumab Superior = 7.9%	Probability Sarilumab Inferior = 86.8%
		Updated Randomization Ratio = 21.9% Sariumab/ 78.1% SOC	
	First Interim Analysis (Additional N=15 Enrolled)	0/5	0/9
		Second Interim Analysis	
		5/19 Total Probability Sarilumab Superior = 5.78%	1/24 Total Probability Sarilumab Inferior = 87.6%
		Updated Randomization Ratio = 19.4% Sarilumab/ 80.6% SOC	
	Follow up After Second Interim Analysis	0/0	0/6
		Third Interim Analysis	
		5/19 total/final	1/30 total/final
		Probability Sarilumab Superior = 3.36%	Probability Sarilumab Inferior = 92.6%
		Study Stopped	
	Limited to Dose Increase to 400 mg (N=41)	2/15	0/25
		Probability Sarilumab Superior = 11.2%	Probability Sarilumab Inferior = 78.6%

Conclusion. This randomized trial of patients hospitalized with COVID-19 and requiring supplemental oxygen but not mechanical ventilation found no evidence of benefit from subcutaneous sarilumab in addition to an evolving standard-of-care. The numbers of patients and events were too low to allow independent conclusions to be drawn, but this study contributes valuable information about the role of subcutaneous IL-6 inhibition in the treatment of patients hospitalized with COVID-19. The major innovation of this trial was the advancement of embedded, point-of-care clinical trials for FDA-approved drugs; this represents a realization of the learning healthcare system. Methods developed and piloted during the conduct of this trial can be used in future investigations to speed the advancement of clinical science.

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518. Model-informed Dose Selection of Dual Toll-like Receptor 7/8 Inhibitor Enpatoran (M5049) for the Treatment of COVID-19 Pneumonia

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