Barplot of Oxygen Delivery Device at Admission and within 28 Days among Treatments

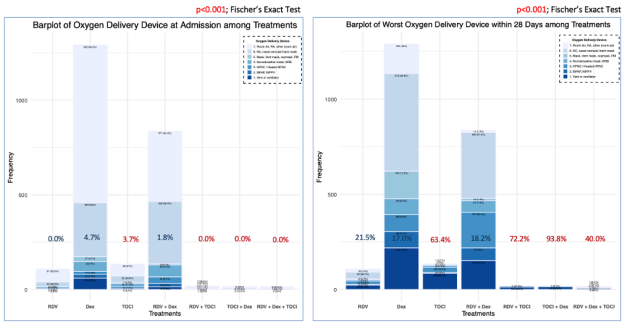

Figure 1. Largest increase in ventilatory support from Day 1 of treatment (left) to Day 28 of treatment (right) was seen among TOCI and DEX (0% to 93.8%), RDV and TOCI (0% to 72.2%) and TOCI alone (3.7% to 63.4%).

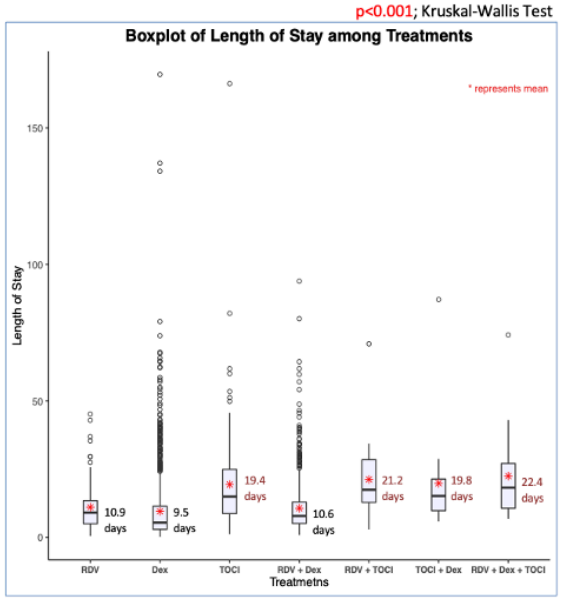

Figure 2. LOS was higher among all treatments containing TOCI (p<0.001), with the highest being the combination group of RDV, TOCI, and DEX (22.4 days, p<0.001).

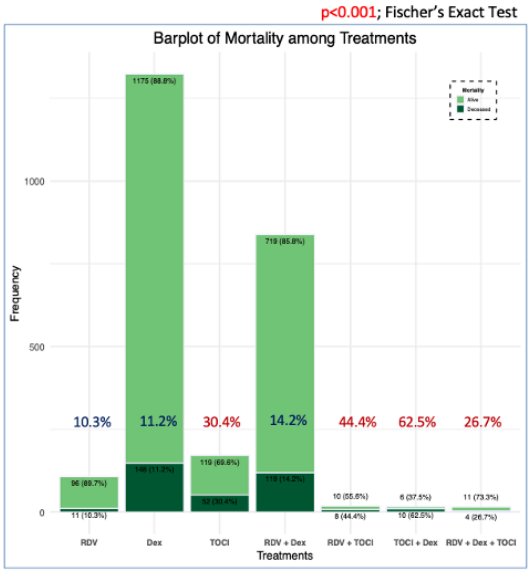

Figure 3. Treatment regimens containing TOCI accounted for the highest mortality rates as seen in TOCI and DEX use (62.5%), RDV and TOCI (44.4%), and TOCI use alone (30.4%).

Conclusion. Our study demonstrates that "real-world" clinical outcomes for patients with COVID-19 treated with Remdesivir, Tocilizumab, and Dexamethasone are consistent with what has been reported in clinical trials. The higher mortality associated with Tocilizumab treatment may reflect the use of this agent in critically ill patients with COVID-19.

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510. Reduced Mortality Rate in Critically Ill Patients with COVID-19 with the Implementation of a Treatment Protocol—Experience of a Tertiary Care Center in the Midwest During the Initial Surge of COVID-19

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Session: P-24. COVID-19 Treatment

Background. COVID-19 has been an unprecedented pandemic resulting in high mortality. We report our experience of using a treatment protocol in the intensive care unit (ICU) during the first peak of the pandemic.

Methods. All patients diagnosed with SARS-CoV-2 infection admitted to the ICU between April 14-June 14, 2020 were included. Remdesivir was made available for use in our institution on May 14th 2020, and thereafter, a treatment protocol combining remdesivir, corticosteroids and tocilizumab was implemented in the ICU, with doses as follows: Remdesivir 200mg intravenously (I.V.) on day 1, then 100 mg for 4 days; tocilizumab 400 mg I.V. once a day for 2 days; dexamethasone 6 mg I.V. daily for 10 days followed by taper. During pre-protocol period, patients were receiving hydroxychloroquine (400 mg once on day 1 followed by 200 mg twice daily orally for 4 days). We compared the pre-protocol period (labeled as P1: April 14, 2020- May 13, 2020) with protocol period (P2: May 14, 2020 -June 14, 2020) for clinical outcomes.

Results. A total of 32 and 48 patients were included during P1 and P2 respectively. Both groups were similar in terms of demographic characteristics, mean (±SD) age [55(±10) and 54 (±12) years] and mean Charlson-Deyo risk score at admission [2.4(±0.8) and 2.5 (±0.9) respectively]. During both periods, a comparable number of patients needed mechanical ventilation (65% and 66% respectively), anticoagulation (74% and 76% respectively) and inotropes (41% and 40%). The mean duration of ICU stay during P1 was significantly longer than P2 [15.4 (±2.8) days versus 9.3 ± (3.8) days, p< 0.0001)]. During P1, mean duration of mechanical ventilation [10 (±1.6) days] was also significantly longer than P2 [7.1 (±2.7) days] (p= 0.0004). There was a significant reduction in mortality rate from 68% (22/32) during P1 to 10.4% (5/48) in P2 (p< 0.0001). Patients were 4.3 times more likely to die during P1 than P2 (95% CI= 2.47-7.86).

Conclusion. Our results showed a decrease in ICU mortality rate by 57.6% with the implementation of a treatment protocol combining remdesivir, tocilizumab and corticosteroids during the first months of the initial surge of the pandemic, with a significant decline in length of ICU stay and duration of mechanical ventilation; and support the therapeutic data endorsed by IDSA/NIH guidelines.

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

511. Treatment with Molnupiravir in the MOVe-In and MOVe-Out Clinical Trials Results in an Increase in Transition Mutations Across the SARS-CoV-2 Genome

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Session: P-24. COVID-19 Treatment

Background. Molnupiravir (MOV), (MK-4482, EIDD-2801) is being clinically developed for the treatment of COVID-19 disease caused by SARS-CoV-2. MOV is the orally administered 5´-isobutyrate prodrug of the active, antiviral ribonucleoside analogue, N-hydroxycytidine (NHC, EIDD-1931) which inhibits viral replication by induction of mutations in the viral genome, leading to viral error catastrophe. In 2 clinical studies, hospitalized (MOVe-In) and non-hospitalized (MOVe-Out) participants were treated for 5 days with MOV and followed up to Day 29. Viral RNA isolated from nasal swab samples were sequenced to determine the rate, distribution and type of viral mutations observed after MOV treatment.

Methods. RNA isolated from nasopharangeal swab samples collected during study conduct was quantified by RT-PCR. Samples containing >22,000 copies/mL of RNA underwent complete genome NGS using the Ion AmpliSeq SARS-CoV-2 research panel and Ion Torrent sequencing. Mutation rates were calculated by determining the number of nucleotide changes observed across the entire genome at Day 3 and/or Day 5 compared to baseline.

Results. Combined data from both studies showed an increase of ~2-4 fold in the viral mutation rate post-baseline in MOV treated compared with placebo. Mutations were distributed across the entire genome with only a minority being observed in more than one sample. The most frequent mutations were transitions of C to U observed in the highest MOV dose group (800 mg/BID).

Conclusion. Consistent with the proposed mechanism of action of MOV, an increase in the rate of transition mutations in the virus was observed in post-baseline nasal swab samples from participants treated with MOV compared with placebo.

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512. Does Time From COVID-19 Symptom Onset to Administration of Anti-spike Protein Monoclonal Antibody Predict Response?

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Session: P-24. COVID-19 Treatment

Background. Casirivimab/imdevimab is a monoclonal antibody (mAb) cocktail with emergency use authorization for mild-to-moderate coronavirus disease 2019 (Covid-19) in patients at high risk for severe disease progression and/or hospitalization. Little is known about the importance of early administration of this product. The objective of this study was to determine if early administration (within 3 days of symptom onset) of casirivimab/imdevimab is associated with better outcomes.

Table 1. Summary of patient characteristics who received casirivimab with imdevimab late or early after patient reported symptom onset

	≥3 days symptoms (n=190)	< 3 days symptoms (n=80)	*P*
Age (years, mean ± SD)	64.5 ± 14.0	62.9 ± 12.7	.356
Days from onset (mean ± SD)	4.8 ± 1.9	1.5 ± 0.7	<.001
BMI (kg/m^2, mean ± SD)	31.1 ± 8.2	31.7 ± 7.3	.598
Female, n (%)	106 (55.8)	43 (53.8)	.758
Caucasian, n (%)	145 (76.3)	59 (73.8)	.901
Hispanic, n (%)	26 (13.7)	12 (15.0)	.776
Oxygen saturation room air (%, mean ± SD)	96.1 ± 2.1	96.5 ± 2.1	.120
Required oxygen, n (%)	11 (10)	7 (16)	.077
Systolic blood pressure (mmHg, mean ± SD)	139.8 ± 20.3	145.0 ± 24.2	.077
Diastolic blood pressure (mmHg, mean ± SD)	79.1 ± 9.9	79.0 ± 10.2	.944
Temperature (°F, mean ± SD)	98.7 ± 1.1	98.6 ± 0.66	.181
Active smoker, n (%)	9 (4.7)	12 (15.0)	.004
Chronic pulmonary disease	25 (13.2)	6 (7.5)	.183
Diabetes, n (%)	47 (24.7)	21 (26.6)	.751
Heart failure, n (%)	3 (1.6)	5 (6.3)	.052
Hypertension, n (%)	70 (36.8)	29 (36.3)	.927
Obese, n (%)	98 (51.6)	42 (52.5)	.890
Charlson-deyo comorbidity index			
≤ 2	180 (94.7)	74 (92.5)	.477
> 2	10 (5.3)	6 (7.5)	.477

Methods. Single-center, retrospective cohort study including all consecutive patients who received casirivimab/imdevimab at our institution through May 2021. The primary outcome was 30-day post-infusion hospital admission rate in patients who received mAb ≥ 3 days (later) or < 3 days (early) in relation to patient reported symptom onset. Secondary outcomes included any hospital revisit within 30-days. Adverse events were also captured. Chi-square and independent samples t-test were used to compare categorical and continuous data, respectively. Multivariable logistic regression was used to adjust for confounders.

Results. 270 patients met the inclusion criteria and were included in the analysis. There were 80 patients with early administration and 190 with later administration. Baseline characteristics for both groups were similar. Mean age was approximately 64 years and BMI 31 mg/m^2. Table 1 provides a summary of patient characteristics. Late and early administration of casirivimab/imdevimab were similar in terms of hospital admission for any therapy related failure within 30 days of mAb administration after adjusting for age and Charlson comorbidity index (3.7% vs. 7.5%; adjusted odds ratio 0.69, 95% confidence interval, 0.20 – 2.39; p=0.561). Similarly, there were no significant differences in any hospital revisit.

Conclusion. We did not find any difference in outcomes between early and late administration of casirivimab/imdevimab.

Disclosures. **Ronald G. Nahass, MD**, **Abbvie** (Grant/Research Support, Speaker's Bureau)**Alkermes** (Grant/Research Support)**Gilead** (Grant/Research Support, Speaker's Bureau)**Merck** (Grant/Research Support, Speaker's Bureau)

513. Use of Antimicrobial Stewardship Program in Operationalizing Monoclonal Antibody Therapy in SARS-CoV-2 Infection

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Session: P-24. COVID-19 Treatment

Background. Antimicrobial stewardship programs (ASP) have been essential during the coronavirus disease 2019 (COVID-19) pandemic response. Use of monoclonal antibodies for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has proven difficult to operationalize, despite being available through emergency use authorization (EUA). Utilizing existing ASP and multidisciplinary approach to lead the effort, we aim to describe our experience in operationalizing monoclonal antibody therapy.

Methods. Retrospective study of SARS-CoV-2 infected adults receiving monoclonal antibody therapy under EUA (December 2020-April 2021). An algorithm developed by the ASP provided education and an interactive online tool allowing referring physicians and patients to assess eligibility prior to hospital arrival. Patients were screened and approved by existing ASP which included; Infectious Disease (ID) physicians, pharmacist, and ID Nurse. A multidisciplinary approach with ER staff and development of pharmacy workflow with order set were utilized as eligible patients received infusion in dedicated ER location. Data such as demographics, co-morbid condition, infusion related complications, hospitalization, and death were reviewed and collected regularly by the ASP team with frequent monitoring and regulatory reporting. Primary patient outcome was preventing hospitalization.

Results. 107 patients received monoclonal antibody therapy. 47% patients were male, 50% White, and 79% non-Hispanic. 87% received monotherapy (bamlanivimab) and 13% received dual therapy (bamlanivimab/etesevimab). 17 patients required hospitalization post infusion. 1 death occurred. COVID-19 related hospitalization within 30-days was avoided in 84% of treated patients. No adverse event directly related to infusion were seen.

Conclusion. Use of monoclonal antibody therapy under EUA for patients for SARS-CoV-2 infection led to decrease in hospitalization in this cohort. An existing ASP using an algorithmic approval process, frequent monitoring, and multidisciplinary approach successfully operationalized the use of monoclonal antibody therapy. ASP's provide benefit and versatility beyond monitoring of antimicrobials alone and should continue to receive support by hospital leadership.

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514. Anti-SARS-CoV-2 Monoclonal Antibodies for Early COVID-19: A Real World Experience

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Session: P-24. COVID-19 Treatment

Background. Anti-SARS-CoV-2 monoclonal antibodies afford prompt immunity, have demonstrated reduction in severe COVID-19 in high risk ambulatory patients, and are available through Emergency Use Authorization. Challenges exist, however, to widespread utilization.

Methods. This operations study 11/23/20-4/30/21 identified patients meeting monoclonal AB EUA criteria by test results or referral. Outreach to harder-hit neighborhoods included connecting with primary care teams and testing sites. Infusion centers with staff trained in infection control, rapid response and drug preparation were utilized. The primary study outcome was treatment of qualifying patients. Secondary outcomes included infusion complications, hospitalization/death, and symptom resolution. Investigational review board approval was obtained.

Results. 367 patients were treated: mean age of 63, 201(55%) male, 276(75%) white, 54(15%) black. All patients had a first positive direct SARS-CoV-2 test within 10 days, 232(63%) had > 1 high-risk qualification, 32(9%) were vaccinated for SARS-CoV-2. Of patients with available zipcodes, 135(38%) had a Community Need Index >3.5 and 157(45%) a Social Vulnerability Index >0.5. 190(52%) received bamlanivimab, 93(25%) casirivimab/imdevimab, 84(23%) bamlanivimab/etesevimab. Four patients experienced infusion reaction, 1 with anaphylaxis. 172(73%) of 236 patients were symptom free at day 5. 20 patients (5%) were hospitalized for COVID-19 within 30 days with a median time from symptom onset to infusion of 7 days, 11(55%) were admitted within 24 hours, 1 died.