

**Conclusion.** A COVID-19 IVDM developed using multiscale MOV virology data supports drug action on viral infectivity and importance of interplay of treatment and immune response and can describe infection time course and drug effect. IVDM provided mechanistic interpretations for VL drug effect in clinical studies.

**Disclosures.** Youfang Cao, PhD, Merck & Co. (Employee) Wei Gao, PhD, Merck & Co., Inc. (Employee, Shareholder) Ruthie Birger, PhD, Merck (Employee) Julie Stone, PhD, Merck & Co., Inc. (Employee, Shareholder)

**524. Assessing the Safety of an Outpatient Remdesivir Infusion Program for Patients with Severe COVID-19 in the Setting of a Pandemic Surge**

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**Session:** P-24. COVID-19 Treatment

**Background.** (i) Remdesivir (RDV) shortens recovery time among COVID-19 patients in an inpatient setting. (ii) Treatments for outpatients diagnosed with COVID-19 are limited. (iii) In early 2021, there was a national surge in COVID-19 hospitalizations, which resulted in hospital bed and staff shortages. (iv) In the face of this pandemic surge, we piloted a program to expand our RDV treatment capacity by establishing an off-label, outpatient infusion tent (OIT) for patients with severe COVID-19. (v) This is a retrospective, descriptive report examining the safety and efficacy of this program, with outcomes of interest being 30-day mortality and hospital admission within the subsequent 30 days

**Methods.** (i) The OIT, consisting of 11 chairs capable of treating 35 patients per day, was operational from January 1 to February 19, 2021. (ii) Patients were referred to the outpatient RDV program primarily from urgent care (UC) and the emergency department (ED), and from the inpatient setting to complete therapy. Patients received at least one dose prior to referral. (iii) Eligibility criteria included a confirmed COVID-19 diagnosis, radiographic evidence of viral pneumonia, and an oxygen saturation less than or equal to 94 on room air. (iv) Exclusion criteria included pregnancy, sepsis, end-stage renal disease or GFR < 30, hepatitis with transaminases 10 times the limit of normal. Patients with BMI > 40, age > 75, chronic lung disease, dementia, were considered on a case by case basis. (v) Patients received dexamethasone and deep vein thrombosis prophylaxis

**Results.** (i) A total of 88 patients received 258 infusions. The average number of outpatient infusions per participant was 2.9. (ii) Four out of 88 patients died (4.5%) within 30 days of first dose in the infusion tent. No deaths occurred in the outpatient setting. (iii) Fourteen out of 88 patients were admitted to the hospital within the subsequent 30 days (15.9%). (iv) 11/14 admissions (78.6%) were due to progression of COVID-19. There were no admissions due to adverse drug reactions

Table 1. Patient Characteristics

Characteristic	N (%)
Sex – Male	57 (64.8%)
Sex – Female	31 (35.2%)
Race/Ethnicity – Black	11 (12.5%)
Race/Ethnicity – Latino	45 (51%)
Race/Ethnicity – White	15 (17.1%)
Age – Median	57.5
BMI – Median	32
BMI > 30	59 (67.1%)
Hypertension	54 (61.4%)
Diabetes I / II	39 (44.3%)
Coronary Artery Disease	6 (6.8%)
Congestive Heart Failure	3 (3.4%)
COPD	5 (5.7%)
Asthma	9 (10.2%)
Chronic Kidney Disease	9 (10.2%)
Chronic Liver Disease	1 (1.1%)

Table 2. Admissions Within Subsequent 30 Days

Reason for subsequent admission	N (%)
Worsening COVID-19 Pneumonia	11 (78.6%)
Pulmonary embolus	1 (7.14%)
Bacteremia	1 (7.14%)
Progression of metastatic cancer	1 (7.14%)

**Conclusion.** Mortality rate in outpatients with severe COVID-19 treated with RDV was similar to that reported in inpatients. In this cohort of patients with severe COVID, a majority (84.1%) avoided hospitalization while still receiving appropriate treatment. Results suggest RDV can be safely delivered to outpatients with severe COVID-19.

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**525. Atovaquone for Treatment of COVID-19 (Ataq COVID-19) Trial**

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**Session:** P-24. COVID-19 Treatment

**Background.** Our group performed an in-silico screen to identify FDA approved drugs that inhibit SARS-COV-2 main protease (Mpro), followed by in vitro viral replication assays, and in vivo pharmacokinetic studies in mice. These studies identified atovaquone as a promising candidate for inhibiting viral replication.

**Methods.** Enrolled patients were randomized in a 2:1 fashion to atovaquone 1500 mg twice daily versus matched placebo. Patients received standard of care treatment including remdesivir, dexamethasone, or convalescent plasma as deemed necessary by the treating team. Patients agreed to allow collection of saliva at baseline and twice a day while hospitalized or up to 10 days. Saliva was collected and RNA extracted for viral load (VL) measurement by Real-time PCR. Our primary outcome was to examine the between group differences in log transformed VL(copies/mL) using generalized linear mixed-effect models of repeated measures from all samples. Additional analysis of Atovaquone plasma concentrations were examined and correlated with viral load and body mass index (BMI).

**Results.** Of the 61 patients enrolled; 41 were received atovaquone and 19 placebo. Overall the population was predominately male Hispanic with a mean age of 51 years. The two groups were balanced (Table 1) with regard to age, gender, race, co-morbidities, days from onset of symptoms, baseline oxygen requirements, and receipt of COVID-19 specific standard of care treatment. A higher proportion with diabetes was noted in the Atovaquone arm. The log<sub>10</sub> VL was 5.25 copies/mL vs. 4.79 copies/mL at baseline in the atovaquone vs. placebo group. Although there was a decrease in VL over time, there was no differences between the atovaquone plus standard of care arm versus the standard of care arm (Figure 1). Additional analysis of atovaquone plasma concentration demonstrated a wide variation in atovaquone levels, inverse association between atovaquone levels and BMI (rho -0.44, p=0.03), and Day 5 concentrations and VL (rho -0.54, p=0.005).

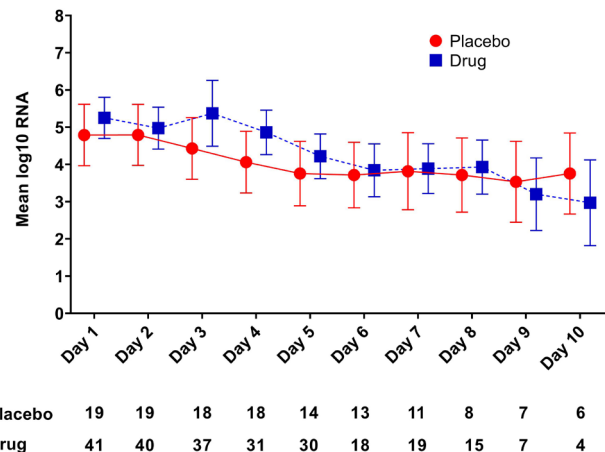


Figure 1. Mean viral load of COVID-19 over time of atovaquone (blue) vs. placebo (red).

Table 1. Baseline characteristics

TABLE 1: Demographics and Clinical Characteristics at Baseline

	Overall	Atovaquone (n=41)	Placebo (n=19)	P value
<b>Gender</b>				
Male	38 (63)	26 (63)	12 (63)	1.0
<b>Race</b>				
White	46 (77)	31 (76)	15 (79)	1.0
Black	8 (13)	6 (15)	2 (11)	
<b>Ethnicity</b>				
Hispanic	42 (70)	29 (71)	13 (68)	1.0
Age, mean years (IQR)	50.9 (41.9, 59.6)	51.64 (42.5, 60.8)	49.4 (41, 59.6)	0.56
BMI, mean (27,36.5)	32.78	32.65(27.1, 35.9)	33.07 (26.8, 37.1)	0.86
<b>Co-morbidities</b>				
Hypertension	38 (63)	26 (63)	12 (63)	1.0
Diabetes	38 (63)	30 (73)	8 (42)	0.04
Obesity	23 (38)	15 (37)	8 (42)	0.78
Chronic kidney disease	20 (33)	12 (29)	8 (42)	0.38
Lung disease <sup>a</sup>	12 (20)	10 (24)	2(11)	0.31
Heart disease <sup>a</sup>	7(12)	5 (12)	2 (11)	1.0
Cancer	6 (10)	3 (7)	3 (16)	0.37
transplant	5 (8)	2 (5)	3 (16)	0.31
liver disease	5 (8)	4 (10)	1 (5)	1.0
Vascular	4 (7)	2 (5)	2 (11)	0.23
Other <sup>b</sup>	3 (5)	1 (2)	2 (11)	0.26
<b>Other treatment</b>				
On remdesivir		27 (66)	9 (47)	0.26
On dexamethasone		30 (73)	14 (74)	1
Plasma		4 (10)	1 (5)	1
<b>Other characteristics</b>				
Days from symptom onset, mean days (IQR)	5.15 (4,6)	5.24 (4,7)	4.95 (4,6)	0.56
<b>Oxygen status at baseline</b>				0.57
Room air	17 (28.3)	10 (24.4)	7 (36.8)	
Low flow oxygen	40 (66.7)	29 (70.7)	11 (57.9)	
High flow oxygen	3 (5)	2 (4.9)	1 (5.3)	

<sup>a</sup> Chronic obstructive pulmonary disease, asthma, smoking

<sup>b</sup> Congestive heart failure, myocardial infarction, coronary artery disease, cardiomyopathy

<sup>c</sup> autoimmune, connective tissue, peptic ulcer, HIV

**Conclusion.** Although atovaquone showed promising in vitro antiviral properties for COVID-19, in this pilot study we did not detect a change in VL in patients who received atovaquone compared to placebo, possibly due to failure of patients achieve adequate drug levels.

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**526. Implementation of Use of Monoclonal Antibody Therapy in a Large Academic Center for the Outpatient Treatment of Covid-19: Impact on 30 Day Hospitalization Rates, ED Visits and Death**

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**Session:** P-24. COVID-19 Treatment

**Background.** Monoclonal Antibody Therapy (MAbs) has been shown to reduce rates of ED visits and hospitalizations in patients at risk for severe Covid-19 infection in clinical trials. Since November, three Mabs received emergency use authorization: Bamlanivimab (Bam), Bamlanivimab/Etesevimab (Bam/Ete) and Casirivimab/Imdevimab (Casi/imdevi). We describe here the real-world effectiveness of implementing early MAb therapy in the outpatient setting for individuals with Covid-19 at high risk of progression.

**Methods.** We examined the records of 808 UCLA Health patients with a confirmed positive SARS-CoV2 PCR test who were either referred for outpatient Mab therapy or received Mab treatment in the emergency department (ED) between December 10, 2020, and May 3, 2021. The primary outcome of our analysis was the combined 30-day incidence of emergency department visits, hospitalizations, or death following the date of referral. SARS-CoV2 isolates of hospitalized patients who had received Mabs were sequenced to determine the presence of variants.

**Results.** Of 808 patients, 383 were referred for treatment but did not receive treatment, 109 received Mabs in the ED and 316 patients were treated in an outpatient setting. Composite 30-day mortality, ED visits and hospital admissions were significantly reduced in the combination therapy group (Bam/Ete or Cas/Imd) compared with monotherapy (Bam alone) or no treatment groups (aHR 0.16, 95% CI .038, .67). Significant factors associated with the composite outcome included: history of lung disease (HR 4.46, 95% CI 2.89-6.90), cardiovascular disease (HR 1.87, 95% CI 1.12-3.12), kidney disease (HR 2.04, 95% CI 1.27-3.25), and immunocompromised state

(HR 3.24, 95% CI 1.02-10.26) as well as high social vulnerability index (HR 1.87, 95% CI 1.13-3.10). Over one-third of hospitalized patients who had received Mabs were confirmed to have the California variant (B.1.427/29) (Figure 1).

Figure 1:

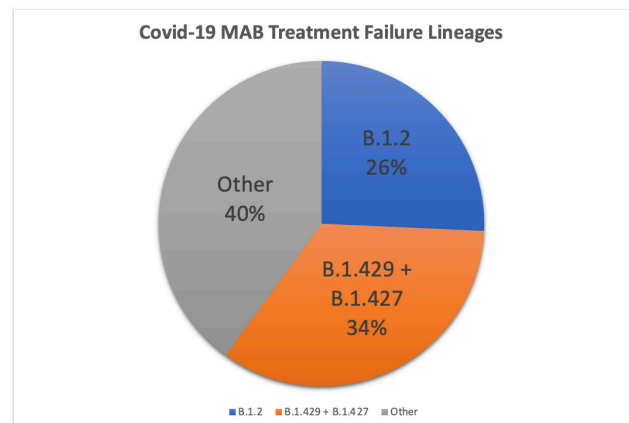


Figure 1. Covid-19 MAB Treatment Failure Lineages

**Conclusion.** Our data show that in a real-world setting, combination monoclonal antibody therapy, not monotherapy, significantly reduced ED visits and hospital admissions, likely due to the presence of the California variants. High socioeconomic vulnerability and certain medical conditions increased risk of treatment failure.

**Disclosures.** Omai Garner, PhD, D(ABMM), Beckman Coulter (Scientific Research Study Investigator)

**527. Lower Risk of ICU Admission with Remdesivir in Patients Hospitalized with COVID-19 Pneumonia**

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**Session:** P-24. COVID-19 Treatment

**Background.** Remdesivir (RDV) was approved by FDA in October 2020 for use in hospitalized patients with COVID-19. We examined the association between RDV treatment and ICU admission in patients hospitalized with COVID-19 pneumonia requiring supplemental oxygen (but not advanced respiratory support) in MN.

**Methods.** COVID-19-Associated Hospitalization Surveillance Network (COVID-NET) is population-based surveillance of hospitalized laboratory confirmed cases of COVID-19. We analyzed COVID-NET cases ≥18 years hospitalized between Mar 23, 2020 and Jan 23, 2021 in MN for which medical record reviews were complete. On admission, included cases had evidence of COVID-19 pneumonia on chest imaging with oxygen saturation < 94% on room air or requiring supplemental oxygen. Cases were excluded if treated with RDV after ICU admission. Multivariable logistic regression was performed to assess the association between RDV treatment and ICU admission.

**Results.** Complete records were available for 8,666 cases (36% of admissions statewide). 1,996 cases were included in the analysis, of which 908 were treated with RDV. 83% of cases were residents of the 7-county metro area of Minneapolis-St. Paul. Mean age was 59.7 years (IQR 48-72), 55% were male, and the mean RDV treatment duration was 4.8 days (range 2-15). The proportion of cardiovascular disease (30.6% vs 23.9%, p=.003), renal disease (16.6% vs 7.6%, p<.001), and diabetes (34.7% vs 29.5%, p=0.01) was higher in the RDV untreated group, while obesity (22.3% vs 8.4%, p<.001) and dexamethasone use (54.7% vs 15%, p<.001) was more common in the RDV treated group. RDV untreated patients were more likely to be admitted to an ICU (18% vs 8.9%, p<.001) and had higher inpatient mortality than those treated with RDV (11% vs 4.4%, p<.001). After adjustment for dexamethasone use, age, sex and diabetes, treatment with RDV was associated with 48% lower odds of ICU admission (OR 0.52, 0.39-0.7, p<.001).

**Conclusion.** We found RDV treatment associated with a significantly lower risk of ICU admission in patients admitted to hospital requiring supplemental oxygen, suggesting that treatment may prevent disease progression in this group. Further studies should assess the potential benefit of RDV combination treatment with dexamethasone.

**Disclosures.** Ruth Lynfield, MD, Nothing to disclose

**528. Hospital Course of Patients Receiving Bamlanivimab: A Real World Analysis**

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