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Session: P-24. COVID-19 Treatment

Background. During the COVID-19 pandemic, the Veterans Affairs Long Beach Healthcare System (VALB HCS) saw a surge of patients with a positive SARS-CoV-2 test. There is a lack of guidance on triaging patients with COVID-19 in the clinical literature. To address this need, our study evaluated factors that predicted hospitalization of patients due to COVID-19.

Methods. This was a retrospective cohort study of patients with a positive SARS-CoV-2 test and medical evaluation at the VALB HCS between August 1 and December 31, 2020. SARS-CoV-2 positive patients admitted to the hospital for a non-COVID-19 related diagnosis were excluded. At the time of initial evaluation, demographic, clinical, and laboratory data, and PCR cycle threshold were collected and compared between patients admitted to the hospital and those managed in the community. A multiple logistic regression analysis was conducted to evaluate predictors for hospitalization due to COVID-19.

Results. Of 748 patients, 94 were admitted to the hospital and 654 were community-managed. The outcomes from the logistic regression analysis indicated that the model explained 58.8% of variance and was a significant predictor of hospitalization (X2 [8, 737] = 277.5, p< 0.0001). Patients with self-reported shortness of breath (OR=12.14, 95% CI=6.43-22.92) or diarrhea (OR=2.78, 95% CI=1.33-5.84) were more likely to be hospitalized, whereas patients with sore throat (OR=0.095, 95% CI=0.017-0.53) or body ache (OR=0.42, 95% CI=0.20-0.89) were less likely to be hospitalized than patients not having such symptoms. Every unit increase in patients' age and temperature increased the likelihood of hospitalization by 7.6% and 62.7%, respectively. Every unit increase in patients' diastolic pressure and SpO_2% decreased the likelihood of hospitalization by 6.1% and 3.6%, respectively.

Conclusion. Our findings indicate that patients with shortness of breath, diarrhea, temperature, and old age were more likely to be hospitalized due to COVID-19. The results may help providers in clinical decision making regarding whether to admit the patient or not. These findings may be especially helpful when hospital bed availability is limited.

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

522. Evaluation of Three COVID-19 Monoclonal Antibody Regimens in the Context of Rising B.1.526 Prevalence in New York City

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Session: P-24. COVID-19 Treatment

Background. Monoclonal antibodies were given emergency use authorization (EUA) by the Food and Drug Administration for the treatment of high-risk, outpatient COVID-19 infection. In New York City (NYC), the emergence and rapid growth of the B.1.526 variant of concern (VOC) possessing the E484K mutation was first noted in February 2021. *In-vitro* studies subsequently confirmed attenuated monoclonal antibody neutralization against VOCs. At our institution, bamlanivimab (BAM) alone or with etesevimab (B/E) and casirivimab/imdevimab (C/I) were utilized at different phases of the pandemic. The objective of this study was to assess their comparative efficacies in a highly variant prevalent setting.

Methods. This retrospective analysis was conducted at an urban hospital in the Bronx, NY and evaluated adult monoclonal antibody recipients from any of our infusion sites. Patients initially received BAM but given the high prevalence of variants, treatment was transitioned to first B/E and then C/I exclusively. We compared BAM versus combination therapy as well as B/E versus C/I individually. The primary outcome was all-cause hospital admission within 30 days post infusion.

Results. From February 1 to March 7, 2021, 358 patients received BAM and from March 17 to May 9, 2021, 86 and 179 patients received B/E and C/I, respectively. Compared to any combination infusion, patients who received BAM were significantly older, more likely to possess ≥ 2 qualifying EUA criteria, and less likely to be vaccinated for COVID-19 prior to infusion (Table 1). Following B/E and C/I, 4.5% of patients were admitted versus 10.1% for BAM, p=0.011. There were no significant differences in admission between B/E and C/I recipients, p=0.485. After excluding fully vaccinated patients (n=14) and adjusting for age and ≥ 2 EUA criteria, combination therapy remained associated with decreased odds of hospitalization compared to BAM (odds ratio, 0.48; 95% confidence interval, 0.24-0.94).

Table 1.

	Combination infusion (n=265)		Bamlanivimab monotherapy (n=358)	*P*-value for comparison of any combination infusion vs monotherapy
	Bamlanivimab/ Etesevimab (n=86)	Casirivimab/ Imdevimab (n=179)		
Male, n (%)	100 (37.7)		150 (41.9)	0.571
	33 (38.4)	67 (37.4)		
Age, years, median (IQR)	57 (45-65)		61 (50-70)	<0.001
	59 (47-68)	56 (44-63)		
Ethnicity or race, n (%)[a]				
Hispanic	104 (42.1)		170 (50)	0.058
	29 (34.9)	75 (45.7)		
Black	79 (32)		75 (22.1)	0.007
	28 (33.7)	51 (31.1)		
White	29 (11.7)		55 (16.2)	0.130
	16 (19.3)	13 (7.9)		
Other	35 (14.2)		40 (11.8)	0.389
	10 (12)	25 (15.2)		
Qualifying EUA criteria, n (%)				
Age ≥65 alone	23 (8.7)		37 (10.3)	0.417
	10 (11.6)	13 (7.3)		
Age ≥65 with comorbidities[b]	45 (17)		102 (28.5)	<0.001
	19 (22.1)	26 (14.5)		
Age 55-64 with comorbidities[b]	60 (22.6)		85 (23.7)	0.748
	14 (16.3)	46 (25.7)		
Body mass index ≥35 kg/m²	100 (37.7)		103 (28.8)	0.018
	32 (37.2)	68 (38)		
Diabetes	90 (34)		132 (36.9)	0.453
	26 (30.2)	64 (35.8)		
Chronic kidney disease	13 (4.9)		19 (5.3)	0.822
	3 (3.5)	10 (5.6)		
Immunosuppression	52 (19.6)		73 (20.4)	0.813
	17 (19.8)	35 (19.6)		
Pregnancy	3 (1.1)		7 (2)	0.529
	1 (1.2)	2 (1.1)		
≥2 EUA criteria[c]	112 (42.3)		188 (52.5)	0.011
	43 (50)	69 (38.5)		
≥3 EUA criteria[c]	40 (15.1)		89 (24.9)	0.003
	10 (11.6)	30 (16.8)		
Symptom duration prior to infusion, days, median (IQR)[a]	6 (4-7)		6 (4-8)	0.165
	6 (4-8)	5 (4-7)		
Received at least 1 dose of COVID-19 vaccine prior to infusion, n (%)	59 (22.3)		16 (4.5)	<0.001
	23 (26.7)	36 (20.1)		
Fully vaccinated prior to infusion[d]	13 (4.9)		1 (0.3)	<0.001
	2 (2.3)	11 (6.1)		
All-cause admission within 30 days post-infusion, n (%)	12 (4.5)		36 (10.1)	0.011[e]
	5 (5.8)	7 (3.9)		
Sensitivity analysis, excluding 75 vaccinated patients	10 (4.9)		35 (10.2)	0.026
	4 (6.3)	6 (4.2)		

[a]Ethnicity or race available for 587 patients, symptom duration available for 596 patients
[b]Comorbidities defined as hypertension, cardiovascular or chronic respiratory condition
[c]Patients with both age > 65 and age > 55 with comorbidities were considered as meeting two separate EUA criteria
[d]Patients were considered fully vaccinated if two weeks had elapsed following receipt of two doses of messenger-RNA vaccines or one dose of viral vector vaccine
[e]*P*=0.485 for bamlanivimab/etesevimab versus casirivimab/imdevimab

Conclusion. Combination therapy may be associated with fewer hospital admissions following infusion, although there were no statistically significant differences between the individual combination infusions. We suggest similar studies be conducted by other sites to understand the clinical impact of local SARS-CoV-2 variants on antibody efficacy.

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523. Use of Immune-Viral Dynamics Modeling to Understand Molnupiravir Drug Effect for COVID-19

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Background. Molnupiravir (MOV) is an orally administered ribonucleoside prodrug of β-D-N4-hydroxycytidine (NHC) against SARS-CoV-2. Here we present viral dynamics analysis of Phase 2 clinical virology data to inform MOV Phase 3 study design and development strategy.

Methods. An Immune-Viral Dynamics Model (IVDM) was developed with mechanisms of SARS-CoV-2 infection, replication, and induced immunity, which together describe the dynamics of viral load (VL) during disease progression. Longitudinal virology data from ferret studies (Cox, et al. Nat. Microbiol 2021:6-11) were used to inform IVDM, which was further translated to human by adjusting parameter values to capture clinical data from MOVe-IN/MOVe-OUT studies. Different placements of drug effects (on viral infectivity vs. productivity) and representations of immune response were explored to identify the best ones to describe data. A simplified 95% drug effect was implemented to represent a highly effective dose of MOV.

Results. IVDM showed data were best described when MOV acts on viral infectivity, consistent with the error catastrophe mechanism of action. A cascade of innate and adaptive immune response and a basal level activation enabled durable immunity and continued viral decay after treatment end. IVDM reasonably describes VL and viral titer data from animals and humans. Influence of MOV start time was explored using simulations. Consistent with the ferret studies, simulations showed when treatment is started within the first week post infection, MOV reduces viral growth, resulting in a lower and shortened duration of detectable VL. When started later (e.g. >7 days since symptom onset), the magnitude of drug effect is substantially diminished in a typical patient with an effective immune response which reduces VL prior to treatment start. Further work is needed to model response in patients with longer term infection, where MOV drug effects may have more persistent utility.