Session: P-24. COVID-19 Treatment

Background. Monoclonal antibodies for the outpatient treatment of the novel Coronavirus Disease 2019 (COVID-19) first received emergency use authorization from the Food and Drug Administration in November 2020. These antibodies have been associated with a reduction in emergency department visits and hospitalization through randomized controlled trials. However, modest data is available to describe the outcomes of patients who were hospitalized despite treatment. This study describes real-world outcomes concerning the treatment of COVID-19 with the first approved monoclonal antibody for COVID-19, bamlanivimab, as well as hospital courses associated with patients admitting after receiving the therapy.

Methods. This single-center, retrospective study evaluated real-world data of patients treated with bamlanivimab. The primary endpoint was a composite of emergency department (ED) visits or hospitalization due to worsening COVID-19. Data was analyzed from November 23, 2020 to March 5, 2021. Descriptive statistics were used to analyze the primary endpoint. Secondary endpoints include reported symptoms 24-hours post-infusion and time to symptom resolution in days. Additionally, clinical course of patients hospitalized were analyzed and include average oxygen requirements, median length of stay, and mortality. A subgroup analysis was conducted between patients less than sixty-five years of age and those sixty-five and older.

Results. 619 patients received bamlanivimab during the specified timeframe. The primary endpoint occurred in 34 patients; 11 ED visits and 23 hospitalizations. Baseline characteristics of the patients hospitalized include median age 69 years (IQR 55, 74), 56.5% male, and 82.6% Caucasian. The most common risk factors for severe disease among those hospitalized were age ≥ 65 years and history of diabetes. The clinical course of hospitalized patients varied but 52.9% required nasal cannula for respiratory support and the average length of stay was 4.5 + 4.5 days. Other COVID-19 therapies included dexamethasone in 76.5% of patients and remdesivir in 47.1% of patients. There were no major differences in the subgroup analysis.

Conclusion. Bamlanivimab appears to attenuate the clinical course of COVID-19 in patients who are hospitalized despite treatment.

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

529. Systematic Review and Meta-Analysis of Ivermectin Safety Profile in COVID-19 Trials

Hannah Wentzel, MPH[1]; Junzheng Wang, BSc (Hons)[1]; Abbienaya Dayanamby, n/a[1]; Victoria Pilkington, BSc MBBS[2]; Jacob Levi, BSc MBBS[3]; Andrew Hill, PhD[4]; Leah Ellis, MPH[5]; [1]Imperial College, London, UK; [2]University of Oxford, Oxford, UK; [3]University College London Hospitals, London, UK; [4]University of Liverpool, London, UK; [5]Imperial College London, London, UK

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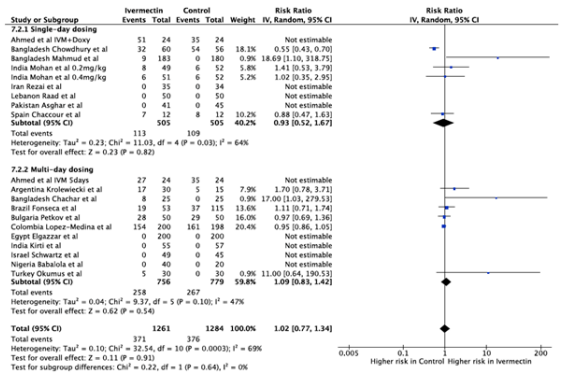
Background. There is a continued and pressing need for safe and effective treatment of COVID-19. Significant survival benefits have been shown by dexamethasone, tocilizumab and sarilumab, however they are only recommended in hospitalised COVID-19 patients. Ivermectin is a well-established and readily available antiparasitic drug which may be suitable for treatment in mild and moderate disease stages. It recently demonstrated anti-viral properties *in vitro* and now over 80 clinical trials have been registered worldwide to test its effectiveness in COVID-19 patients. This meta-analysis aims to collect data on adverse events reported in new COVID-19 treatment trials for the use of ivermectin as a repurposed medication.

Methods. Data was extracted from randomised trials of COVID-19 treatment trials identified through systematic searches of PUBMED, EMBASE, MedRxiv and trial registries. The primary outcome of this meta-analysis is the frequency of adverse events. Key safety events included serious, gastrointestinal, neurological, cardiovascular and dermatological adverse events.

Results. Overall, 18 trials investigating ivermectin for COVID-19 in a total of 2496 participants reported safety data and were included. There was no significant difference in the proportion of all adverse events between ivermectin and the comparator. There were 371/1261 (29%) adverse events recorded in the ivermectin containing arms and 376/1284 (29%) in the control arms (RR 1.02 [95% CI 0.77 - 1.34]; p = 0.91). There was no significant difference in the rate of serious adverse events across treatment arms (RR 1.95 [95% CI 0.75 - 5.11]; p = 0.18). No significant differences between ivermectin and the control were seen across different subcategories of adverse events. Figure 1 shows a summary of the results for all adverse events.



Forest plot comparing ivermectin and the control for all adverse events in COVID-19 trials, subdivided into single-day dosing trials and multi-day dosing trials.

Conclusion. The results of recent COVID-19 trials show that overall, ivermectin is safe and well-tolerated. No significant difference in adverse event reporting was found across all subgroups in single and multi-day treatment regimens for the studies analysed. Safety reporting methodologies often varied across trials. Future and ongoing trials should be encouraged to collect and monitor safety data systematically.

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

530. Bamlanivimab (BAM) for SARS-CoV-2 Infection: Rates and Risk Factors for Hospitalization after Monoclonal Antibody Administration in a High-Risk Population

John M. Curtin, MD[1]; Varea H. Costello, DO[1]; Benjamin L. Custer, M.D.[1]; Jason M. Blaylock, MD[2]; Catherine F. Decker, MD[3]; Roseanne Ressner, DO[4]; Sara Robinson, MD[4]; Wesley R. Campbell, MD, MTM&H[1]; Dana M. Blyth, MD[1]; Dana M. Blyth, MD[1]; Anuradha Ganesan, MBBS, MPH[5]; [1]Walter Reed National Military Medical Center, North Bethesda, Maryland; [2]Walter Reed National Military Medical Center, Bethesda,, Bethesda, Maryland; [3]WRNMMC/USU, Bethesda, Maryland; [4]Walter Reed National Military Medical Center, Bethesda, MD, Bethesda, Maryland; [5]Infectious Disease Clinical Research Program and the Henry M. Jackson Foundation for the Advancement of Military Medicine and Walter Reed National Military Medical Center, Bethesda, MD

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Background. In response to the ongoing COVID-19 pandemic, an emergency use authorization (EUA) was issued for neutralizing antibody therapies including BAM. Licensing trials suggest that use of BAM reduces hospitalizations when compared with placebo (1.6% vs 6.3%). However, the real world impact of BAM is not well-described. In this study, risk factors, outcomes, and hospitalization rates among high-risk outpatients presenting with mild-to-moderate COVID-19 who received BAM were examined.

Methods. This is a single center retrospective analysis of all patients who received BAM monotherapy between 11/11/2020 and 3/16/2021. Electronic health records were reviewed for baseline demographics, EUA indications, comorbidities, and outcomes to include infusion reactions, hospitalizations, and deaths occurring within 29 days of BAM administration. Moderate COVID-19 was defined as having any infiltrate on chest imaging prior to BAM administration. Chi-squared or Fisher's exact tests were used to compare categorical values as appropriate, and Mann-Whitney U for continuous variables.

Results. Of the 101 patients who received BAM (median age 64 years; 21% black; 4% Hispanic; 55% male), 13 were subsequently admitted. 22 patients (22%) had moderately severe disease as evidenced by abnormal imaging. Severity on presentation, number of indications for therapy, hypertension, stroke, diabetes, and number of co-morbidities were significantly associated with subsequent admission (table 1). No patients had adverse infusion reactions. Of those hospitalized, 8 (61.5%) were for COVID-19, the median duration of hospitalization was 2 days, and 4 received guideline-directed treatment for COVID-19 (table 2).

Table 1. Factors Associated with Hospitalization Following Bamlanivimab (BAM) Administration

Characteristic	Total n=101 (%)	No admission n=88 (%)	Admissions n=13 (%)	P value
Age, median (IQR) in years	64 (57, 71)	64 (57, 71)	63 (59, 73)	0.711
Male Sex	56 (55%)	48 (54%)	8 (62%)	0.636
Race				0.358
Black	21(21%)	16 (18%)	5 (39%)	
White	48 (48%)	44 (50%)	4 (31%)	
Asian	3 (3%)	3 (3%)	0	
Hispanic	4 (4%)	4 (5%)	0	
Unknown/Other	25 (25%)	21 (24%)	4 (31%)	
BMI, median (IQR)	30 (25.6, 35)	30 (25.55, 35)	30.27 (26, 34.5)	0.988
BMI by obesity class				0.753
Normal	16 (16%)	15 (17%)	1 (8%)	
Overweight	32 (32%)	27 (31%)	5 (39%)	
Obesity class 1	24 (24%)	20 (23%)	4 (31%)	
Obesity class 2	27 (27%)	24 (27%)	3 (23%)	
Obesity class 3	0	0	0	
Indication for mAb admin				
BMI≥35[¥]	28 (28%)	25 (28%)	3 (23%)	0.754
CKD	15 (15%)	12 (14%)	3 (23%)	0.404
DM	35 (35%)	26 (30%)	9 (69%)	0.010
Immunosuppressive conditions	31 (31%)	27 (31%)	4 (31%)	1.000
Age ≥65	47 (47%)	42 (48%)	5 (39%)	0.532
Age ≥55 with cardiovascular disease, hypertension, or chronic respiratory disease	6 (6%)	5 (6%)	1 (8%)	0.572
Number of Indications for mAb, median (IQR)	2 (1,2)	1 (1,2)	2 (2,2)	0.010
COVID-19 severity±				0.023
Mild	79 (79%)	72 (82%)	7 (54%)	
Moderate	22 (22%)	16 (18%)	6 (46%)	
Days of symptoms prior to COVID 19 testing, median (IQR)	2 (1,3)	2 (1,3)	2 (1,3)	0.423
Days of symptoms prior to mAb administration, median (IQR)	4 (2,5)	4 (2, 5.25)	2 (1,4)	0.182
Days from positive test to BAM, median (IQR)	1 (0,2)	1 (0,2)	0 (0,1)	0.085
Symptoms				
Cough	66 (66%)	58 (66%)	8 (62%)	0.757

Table 1. (Continued) Factors Associated with Hospitalization Following Bamlanivimab (BAM) Administration

Dyspnea	32 (32%)	25(28%)	7 (54%)	0.067
Fever	53 (53%)	44 (50%)	9 (69%)	0.159
Diarrhea	12 (12%)	11 (13%)	1 (8%)	1.000
Fatigue	56 (56%)	48 (55%)	8 (62%)	0.636
Comorbidities:				
Asthma	6 (6%)	5 (6%)	1 (8%)	0.572
Chronic Obstructive Lung Disease	4 (4%)	4 (5%)	0	1.000
Coronary Artery Disease	9 (9%)	9 (10%)	0	0.600
Deep Vein Thrombosis	2 (2%)	1 (1%)	1 (8%)	0.242
Pulmonary Embolism	2 (2%)	1 (1%)	1 (8%)	0.242
Hypertension	64 (64%)	52 (59%)	12 (92%)	0.028
Malignancy	9 (9%)	9 (10%)	0	0.600
Rheumatological Disease	16 (16%)	13 (15%)	3	0.428
History of Stroke	3 (3%)	1 (1%)	2 (15%)	0.043
Peripheral Arterial Disease	1 (1%)	1 (1%)	0	1.000
Smoking status				0.120
Non-smoker	91 (91%)	81 (92%)	10 (77%)	
Current	2 (2%)	1 (1%)	1 (8%)	
Former	7 (7%)	5 (6%)	2 (15%)	
Organ Transplant	3 (3%)	2 (2%)	1 (8%)	0.342
Number of co-morbidities, median (IQR)*	2 (1,3)	2 (1,2)	3 (2,3)	0.013
Number of co-morbidities				0.073
0 comorbidities *	9 (9%)	9 (10%)	0	
1 comorbidity	29 (29%)	27 (31%)	2 (15%)	
2 comorbidities	37 (37%)	33 (38%)	4 (31%)	
≥3 comorbidities	26 (26%)	19 (22%)	7 (54%)	

[¥] BMI status was missing for two patients. *Age >65 was the only reason for administration of bamlanivimab. †Moderate disease defined as COVID-19 positive with any infiltrate on chest imaging.

Table 2: Characteristics and Resource Utilization of Patients Hospitalized After Bamlanivimab Therapy (n=13)

														Total (%)	Median (IQR)
Patient #	1	2	3	4	5	6	7	8	9	10	11	12	13		
Age/Gender	57/F	59/M	86/M	59/M	60/M	61/M	78/F	56/M	63/M	73/F	41/F	61/M	73/F	-	65 (59,73)
Primary Indication for admission	Chest pain	Syncope	Dyspnea	Pneumonia	Pneumonia	Hyponatremia	Respiratory Failure	Dyspnea	Observation	Weakness	Bacteremia	Weakness	Pneumonia	-	-
COVID-associated indication for admission	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	8 (61.5)	-
Number of days from symptom onset to admission	15	3	15	3	15	4	14	6	2	13	2	3	11	-	6 (3,14)
Number of days from positive testing to admission	16	0	14	3	15	2	12	1	1	10	1	1	5	-	3 (1,12)
Number of days following mAb administration to admission	14	0	13	3	6	0	12	1	1	10	1	1	4	-	3 (1,10)
Duration of hospitalization	1	2	5	16	1	1	4	2	1	4	2	3	6	-	2 (1,4)
Highest ordinal scale during admission*	4	4	5	5	4	4	5	5	4	4	4	4	4	-	4 (4,5)
Ordinal scale 72 hours after discharge*	1	1	1	1	1	1	2	1	1	1	1	1	1	-	1 (1,1)
Intubation during hospitalization	No	No	No	No	No	No	No	No	No	No	No	No	No	0	-
Duration of oxygen during hospitalization, days	-	-	1	4	-	-	3	2	-	-	-	-	-	-	2.5 (1.75, 3.25)
Remdesivir Administered	No	No	No	Yes	No	No	Yes	Yes	No	Yes	No	No	No	4 (30.7)	-
Glucocorticoids Administered	No	No	No	Yes	No	No	Yes	Yes	No	Yes	No	No	No	4 (30.7)	-
Other COVID-19 Therapy¥	No	No	No	No	No	No	No	No	No	No	No	No	No	0	-
Readmission	No	No	No	No	No	No	No	No	No	No	No	No	No	0	-
Death	No	No	No	No	No	No	No	No	No	No	No	No	No	0	-

*Ordinal scale defined in accordance with ACTT-1 trial as follows: 1, not hospitalized and no limitations of activities; 2, not hospitalized, with limitation of activities, home oxygen requirement, or both; 3, hospitalized, not requiring supplemental oxygen and no longer requiring ongoing medical care (used if hospitalization was extended for infection-control or other nonmedical reasons); 4, hospitalized, not requiring supplemental oxygen but requiring ongoing medical care (related to Covid-19 or to other medical conditions); 5, hospitalized, requiring any supplemental oxygen; 6, hospitalized, requiring noninvasive ventilation or use of high-flow oxygen devices; 7, hospitalized, receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); and 8, death. ¥Other COVID-19 therapy included any emergency use authorized COVID-19 directed medications except remdesivir and steroids.

Conclusion. In a high-risk population, hospitalization rates were higher than those observed in clinical trials, with 8% of subjects being admitted for COVID-19. Disease severity on presentation, multiple indications for therapy, and the presence of multiple co-morbidities were all associated with subsequent admission. Reassuringly, BAM was well tolerated, and in those requiring admission, hospitalizations were short, resource utilization was low, and there were no deaths.

Disclosures. **Benjamin L. Custer, M.D.**, Alexion Pharmaceuticals (Shareholder) Armata Pharmaceuticals (Shareholder)Biomarin Pharmaceutical (Shareholder) Crispr Therapeutics (Shareholder)CVS Health Corp (Shareholder)Editas Medicine (Shareholder)Gilead (Shareholder)Glaxo Smith Kline (Shareholder)Hologic Inc (Shareholder)Merck (Shareholder)Mesoblast LTD (Shareholder)Pfizer (Shareholder) Sanofi (Shareholder)Unitedhealth Group (Shareholder)Vertex Pharmaceuticals (Shareholder) **Dana M. Blyth, MD**, Nothing to disclose

531. Risk Factors and Therapeutic Interventions Associated with Mortality in Veterans Diagnosed With SARS-CoV-2 Infection (or COVID-19) Admitted to a Large Academic Medical Center

Elwyn Welch, PharmD[1]; Shazia Raheem, PharmD[2]; Andrew Hunter, PharmD, BCPS (AQ-ID)[3]; Uma Ayyala, MD[2]; Venkata Bandi, MD[2]; Lavannya Pandit, MD[2]; Christina Kao, MD, PhD[2]; [1]Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas; [2]Michael E. DeBakey Veterans Affairs Medical Center/Baylor College of Medicine, Houston, Texas; [3]Michael E DeBakey VA Medical Center, Houston, TX

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Background. Patient and treatment-related factors have been used to stratify COVID-19 outcomes; however, studies in the general population and specifically veterans have yielded variable results. This study was designed to assess how baseline characteristics and interventions correlate with clinical outcomes in patients admitted with COVID-19 at a large academic Veterans Affairs hospital.

Methods. Retrospective chart review was conducted on veterans admitted to the hospital with COVID-19 between March 1 to December 31, 2020. Veterans without respiratory symptoms attributed to COVID-19 or enrolled in a COVID-19 clinical trial were excluded. Primary outcome was in-hospital mortality up to 28 days. Secondary outcomes were 90-day mortality, discharge to higher level of care or remained in the hospital within 28 days, and discharge with new oxygen requirement within 28 days. Patient characteristics and therapeutic interventions were assessed for correlation with primary and secondary outcomes.

Results. Of 497 hospitalized patients reviewed, 293 were included for analysis; 94% were male; average age was 68 years with 64.9% of veterans greater than 65 years of age; 43.7% were Black; 17.4% were Hispanic. In-hospital mortality at 28-days and 90-day mortality were 18.1% and 21.5%, respectively. At discharge, 34.1% had a new oxygen requirement and 17.5% went to a higher level of care. Patients that died in-hospital were more likely to be greater than 65 years of age (p< 0.001), Hispanic (p=0.007), have chronic kidney disease (CKD) (p=0.005), be admitted to ICU (p< 0.001); receive dexamethasone (p< 0.001), convalescent plasma (p< 0.001), or antibiotics (p< 0.001); require mechanical ventilation (p< 0.001); or have new onset atrial fibrillation (p< 0.001). Veterans also had higher levels of inflammatory markers within 48 hours of hospital admission (see Table 2) and longer length of hospital stay (< 0.001). There was a trend for patients that died in the hospital within 28-days to be less likely to be Black (p=0.06).

Table 1. Primary and Secondary Outcomes of Study Population (n=293)

Outcomes all patients – no. (%)	N =293
In-hospital mortality within 28 days	53 (18.1)
90-day mortality	63 (21.5)
28-day outcomes in survivors– no. (%)	n =240
New oxygen requirement at hospital discharge	82 (34.1)
Discharge to similar or lower acuity setting	198 (82.5)

Table 2. Patient Characteristics Stratified by Primary Outcome

	Total Study Population (n=293)	Survivors (n=240)	Nonsurvivors (n=53)	p-value
Male sex – no. (%)	275 (94)	225 (93.8)	50 (94.3)	0.87
Age				
Mean – yr ± SD	68 ± 14	66 ± 14	75 ± 10	*<0.001*
≤ 65 yr	103 (35.2)	97 (40.4)	6 (11.3)	*<0.001*
> 65 yr	190 (64.9)	143 (59.6)	47 (88.7)	
BMI, kg/m² (n=284)	29.8 ± 6.6	29.9 ± 6.8	29.6 ± 5.6	0.79
Race or ethnic group – no. (%)				
Caucasian	153 (52.2)	199 (49.6)	34 (64.2)	0.055
Black	128 (43.7)	111 (46.2)	17 (32.1)	0.06
Hispanic	51 (17.4)	34 (14.2)	17 (32.1)	*0.007*
Co-Morbidities – no. (%)				
Hypertension	217 (74.1)	177 (73.8)	40 (75.5)	0.80
Chronic Kidney Disease	154 (52.6)	117 (48.8)	37 (69.8)	*0.005*
Diabetes mellitus	150 (51.2)	117 (48.8)	33 (62.3)	0.08
Atrial fibrillation	55 (18.8)	41 (17.1)	14 (26.4)	0.12
Heart Failure	48 (16.4)	36 (15)	12 (22.6)	0.17
Chronic Obstructive Pulmonary Disease	38 (13.0)	34 (14.2)	4 (7.6)	0.19
Immunosuppression	35 (11.9)	25 (10.4)	10 (18.9)	0.086
Venous thromboembolism	19 (6.5)	15 (6.3)	4 (7.6)	0.73
Malignancy	18 (6.1)	13 (5.4)	5 (9.4)	0.27
Connective Tissue Disease	10 (3.4)	7 (2.9)	3 (5.7)	0.32
Current or former smoker – no. (%)	95 (32.5)	81 (33.9)	14 (26.4)	0.29
Median Laboratory values within 48 hours (IQR)				
C-reactive protein level, mg/liter (n=175)	75 (42, 171)	69 (37, 147)	165 (76, 196)	*<0.001*
D-dimer level, µg/mL (n=202)	1.14 (0.64, 1.96)	1.0 (0.6, 1.8)	1.4 (0.9, 4.4)	*0.004*
Ferritin level, ng/mL (n=206)	468 (236, 793)	445 (220, 765)	512 (364, 954)	0.07
Procalcitonin level, ng/mL (n=190)	0.13 (0, 0.4)	0.11 (0, 0.31)	0.31 (0.13, 0.68	*<0.001*
Troponin level, ng/mL (n=274)	0 (0, 0.05)	0 (0, 0.04)	0.05 (0, 0.19)	*<0.001*
Treatments – no. (%)				
Eligible for Remdesivir*	235 (80)	154 (64.2)	36 (67.9)	0.60
Received Remdesivir (n=235)	190 (80.8%)	161 (67.1)	42 (79.3)	0.082
Dexamethasone	203 (69.3)	142 (59.2)	49 (92.5)	*<0.001*
Convalescent Plasma	84 (28.7)	86 (35.8)	35 (66.0)	*<0.001*
Antibiotics	191 (65.2)	52 (21.7)	32 (60.4)	*<0.001*
Therapeutic Anticoagulation	121 (41.3)	154 (64.2)	36 (67.9)	0.60
Outcomes				
Median Hospital LOS, days (IQR)	8 (5, 14)	7 (4, 12.5)	14 (9, 21)	*<0.001*
ICU Admission – no. (%)	59 (20.1)	20 (8.3)	39 (73.6)	*<0.001*
Mechanical Ventilation – no. (%)	35 (12.0)	7 (2.9)	28 (52.8)	*<0.001*
New onset atrial fibrillation – no. (%)	21 (7.2)	11 (4.6)	10 (18.9)	*<0.001*
New onset venous thromboembolism – no. (%)	18 (6.1)	14 (5.8)	4 (7.6)	0.64

*Prior to FDA approval, patients eligible for remdesivir determined by emergency use authorization criteria; after FDA approval, patients eligible for remdesivir determined by criteria for use determined by VA