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ABOUT COVER

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The primary aim of *World Journal of Virology* (*WJV*, *World J Virol*) is to provide scholars and readers from various fields of virology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJV mainly publishes articles reporting research results obtained in the field of virology and covering a wide range of topics including arbovirus infections, viral bronchiolitis, central nervous system viral diseases, coinfection, DNA virus infections, viral encephalitis, viral eye infections, chronic fatigue syndrome, animal viral hepatitis, human viral hepatitis, viral meningitis, opportunistic infections, viral pneumonia, RNA virus infections, sexually transmitted diseases, viral skin diseases, slow virus diseases, tumor virus infections, viremia, and zoonoses.

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META-ANALYSIS

Efficacy and safety of bamlanivimab in patients with COVID-19: A systematic review and meta-analysis

Behnam Amani, Lida Khodavirdilou, Kourosh Rajabkhah, Vida Kardan Moghaddam, Arash Akbarzadeh, Bahman Amani

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Abstract

BACKGROUND

Monoclonal antibodies (mAbs) have shown clinical benefits against coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Several studies have reported the use of bamlanivimab as a promising treatment option for COVID-19.

AIM

To synthesize the latest evidence for the efficacy and safety of bamlanivimab alone in the treatment of adult patients with COVID-19.

METHODS

A literature search was conducted in PubMed, Cochrane Library, Web of Science, medRxiv, and Google Scholar using "SARS-CoV-2", "COVID-19", "LY-CoV555", and "Bamlanivimab" keywords up to January 25, 2023. The quality of included studies was assessed using the Cochrane bias tools. The Comprehensive Meta-Analysis software version 3.0 was used to analyze the data.

RESULTS

A total of 30 studies involving 47368 patients were included. A significant

difference was observed between the bamlanivimab and standard of care/placebo groups in terms of mortality rate [risk ratio (RR) = 50, 95% confidence interval (CI): 0.36-0.70], hospitalization rate (RR = 0.51; 95%CI: 0.39-0.68), and emergency department (ED) visits (RR = 0.69; 95%CI: 0.47-0.99); while the two groups exhibited no significant difference in terms of intensive care unit (ICU) admission ($P > 0.05$). Compared to other mAbs, bamlanivimab was associated with a higher rate of hospitalization (RR = 1.44; 95%CI: 1.07-1.94). However, no significant difference was detected between the bamlanivimab and other mAbs groups in terms of mortality rate, ICU admission, and ED ($P > 0.05$). The incidence of any adverse events was similar between the bamlanivimab and control groups ($P > 0.05$).

CONCLUSION

Although the results suggest the efficacy and safety of bamlanivimab in COVID-19 patients, further research is required to confirm the efficacy of this drug for the current circulating SARS-CoV-2 variants.

Key Words: SARS-CoV-2; COVID-19; Bamlanivimab; Monoclonal antibody; Meta-analysis

Core Tip: The present study is the most comprehensive systematic review and meta-analysis on the efficacy and safety of bamlanivimab in the treatment of coronavirus disease 2019 (COVID-19). A significant difference was observed between the bamlanivimab and standard of care/placebo groups in terms of mortality rate, hospitalization rate, and emergency department visits. While the two groups exhibited no significant difference in terms of intensive care unit admission. The present results suggested that bamlanivimab might be effective and safe for the treatment of COVID-19.

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INTRODUCTION

Despite a high rate of vaccination, cases of breakthrough coronavirus disease 2019 (COVID-19) have been reported worldwide[1]. Consequently, numerous pharmaceutical interventions have been proposed to prevent and manage severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the primary cause of COVID-19[2]. Numerous clinical studies have demonstrated that various monoclonal antibodies (mAbs), including sotrovimab[3], casirivimab/imdevimab[3,4], cilgavimab/tixagevimab[5], regdanvimab[6], bamlanivimab/etesevimab[7], and bamlanivimab[8] could be potentially effective in reducing mortality and morbidity in patients with mild to moderate COVID-19. These interventions specifically target the spike protein of the SARS-CoV-2 virus, thereby, inhibiting its activity[9]. In particular, bamlanivimab has been approved by the United States Food and Drug Administration (FDA) for the treatment of non-hospitalized patients with mild to moderate COVID-19[10]. It is worth noting that the FDA has recently revoked the authorization of bamlanivimab for the treatment of COVID-19 due to the emergence of SARS-CoV-2 variants that are resistant to this particular mAbs[11]. However, bamlanivimab is still used in combination with etesevimab for the management of mild to moderate COVID-19 in individuals at high risk of developing severe symptoms[12]. Multiple studies have shown that the administration of bamlanivimab is strongly associated with a notable decrease in the risk of mortality, lower hospitalization rates, and a decreased likelihood of intensive care unit (ICU) admission compared to treatment options that do not include mAbs[8,13,14]. However, the effectiveness of anti-SARS-CoV-2 mAb agents against the Omicron variant of the virus has some concerns[15]. Therefore, the objective of this study is to compile and analyze the available evidence regarding the effectiveness and safety of bamlanivimab in the treatment of patients with COVID-19.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses was utilized as a reporting guideline for conducting this systematic review and meta-analysis of primary studies[16].

Literature search

An extensive literature search was conducted to gather relevant evidence. The search was performed in PubMed, Cochrane Library, Web of Science, medRxiv, and Google Scholar, up to January 25, 2023. Apart from the database search, the reference lists of the included studies were also examined to identify any additional relevant records. No language restrictions were applied. The search strategy in PubMed included keywords such as "Coronavirus", "COVID-19",

"SARS-CoV-2", "Bamlanivimab", and "LY-CoV555". The specific search strategy in PubMed was as follows: (((((((Coronavirus[Title/Abstract]) OR (Coronavirus[MeSH Terms])) OR (COVID-19 [Title/Abstract])) OR (SARS-CoV-2 [Title/Abstract])) OR (COVID-19[MeSH Terms])) OR (SARS-CoV-2 [MeSH Terms])) OR (2019 novel coronavirus infection[Title/Abstract])) OR (2019-nCoV infection[Title/Abstract])) AND ((Bamlanivimab [Title/Abstract] OR (LY-CoV555 [Title/Abstract]).

Selection study

To be included in the study, the selected studies had to meet the following criteria: (1) Addressing adult patients who with positive COVID-19 results based on the polymerase chain reaction test; (2) Bamlanivimab alone as treatment; (3) Using placebo (PBO), standard of care (SOC), and other therapeutic interventions as the control group; and (4) Addressing mortality rate, hospitalization rate, emergency department (ED) visits, ICU admission rate, and incidence of adverse events as the measures of efficacy and safety. Animal studies, case reports, letters to the editor, and studies that did not report relevant outcomes were excluded from the analysis.

Risk of bias assessment

Two authors independently assessed the bias risk in observational studies and randomized controlled trials (RCTs) using Nonrandomized Studies of Interventions (ROBINS-I) tool and Cochrane Risk of Bias (ROB) tool, respectively[17,18].

Data extraction

Two authors independently extracted the following data from the included studies: (1) Study characteristics including information such as the name of the first author, year of publication, location of the study, and study design; (2) Participant characteristics such as sample size, sex distribution, and the mean age of the participants; (3) Intervention and control including details on the sample size of both intervention and control groups, and the treatment dosage and duration; and (4) Efficacy and safety outcomes consisted of the reported efficacy (*i.e.*, mortality rate, hospitalization rate, ED visits, ICU admission rate, and the incidence of adverse events). By independently extracting this data, the authors ensured a thorough and accurate collection of information for analysis.

Data analysis

The Comprehensive Meta-Analysis software was employed to compare the efficacy and safety between bamlanivimab and the control groups. The risk ratio (RR), along with a 95% confidence interval (CI), was employed to analyze the dichotomous variables. The level of heterogeneity was assessed using the I^2 statistic, with a value greater than 50% or a *P*-value less than 0.1, indicating high heterogeneity ($I^2 > 50\%$ or $P < 0.1$). A random-effects model was employed in highly heterogeneous studies, while a fixed-effects model was used for studies with low heterogeneity. Both RCTs and observational studies were analyzed together to estimate the effect size. Subgroup analyses were conducted based on the age of patients (less than 65 years or 65 and over), sample size, and study design. Moreover, a sensitivity analysis was performed by excluding studies with remarkable risk of bias for outcomes of mortality rate and hospitalization rate. Publication bias was assessed by Begg's test and Egger's test.

RESULTS

Figure 1 depicts the study selection process, starting from the initial literature search, removal of duplicates, and screening based on title, abstract, and full-text. Out of the initial 584 studies identified after removing duplicates, 49 full-text studies were considered for eligibility assessment. Ultimately, a total of 30 studies with 47368 patients were included in the meta-analysis[8,10,11,13,14,19-43]. Excluded studies are presented in Figure 1 along with their corresponding reason. The majority of the included studies were of retrospective nature and conducted in the United States. Furthermore, most of the studies were published in 2021, coinciding with the SARS-CoV-2 Delta wave. COVID-19 vaccination status was reported in a few number of studies. Studies mainly evaluated the efficacy of bamlanivimab in patients with mild-to-moderate COVID-19 infection. In most studies, bamlanivimab was administered at a dose of 700 mg. In some studies, however, patients received doses of 2800 and 7000 mg. More detailed information on the characteristics of the included studies is listed in Table 1.

Risk of bias assessment

Supplementary Tables 1 and 2 respectively show the risk of bias assessment determined by ROB and ROBINS-I tools. Accordingly, the included studies had acceptable quality.

Efficacy outcomes

Mortality rate: The pooled estimate revealed a significant difference in mortality rate of the bamlanivimab compared to the SOC/PBO groups (RR = 0.50; 95%CI: 0.36-0.70, $P < 0.05$, $I^2 = 15\%$) (Figure 2A). However, no significant difference was observed between bamlanivimab and other mAbs in terms of mortality rate (RR = 1.71; 95%CI: 0.85-3.44, $P = 0.12$, $I^2 = 0\%$) (Supplementary Figure 1).

Hospitalization rate: A significant difference was observed in the hospitalization rate of bamlanivimab-receiving patients compared to those treated with SOC/PBO (RR = 0.51; 95%CI: 0.39-0.68, $P < 0.05$, $I^2 = 80\%$) (Figure 2B). Moreover, a

Table 1 Main characteristic of included studies

Ref.	Country	Design	Sample size	Male %	Severity of COVID-19	Bamlanivimab			Comparison(s)			
						n	Mean age	Comorbidity[1]	Name	*n*	Mean age	Comorbidity[1]
Alam *et al*[19], 2021	United States	RS	264	44	MM	160	81	58.1	SOC	86	84	51.2
Bariola *et al*[13], 2021	United States	RS	1392	44.39	MM	232	67.3	75.9	SOC	1160	67.1	73.6
Brock *et al*[20], 2021	United States	RS	108	NA	MM	58	NA	100	SOC	58	NA	100
Chen *et al*[21], 2021	United States	RCT	24	54	MC	18	NA	NA	PBO	6	43.2	NA
Chen *et al*[21], 2021	United States	RCT	452	44.9	MM	309	45	69.6	PBO	143	46	66.4
Chew *et al*[23], 2022	United States	RCT	317	51.1	MS	159	NA	NA	PBO	158	NA	NA
Cooper *et al*[24], 2021	United States	RS	5758	45.13	NA	1718	60	56.3	SOC, B/E, C/I	4040	NA	> 50
Corwin *et al*[25], 2021	United States	RS	6117	42.7	MM	780	62.6	68.1	SOC	5337	56.7	47.1
Destache *et al*[14], 2021	United States	RS	234	47	MM	117	72	69.2	SOC	117	72	63.3
Djuric *et al*[26], 2022	Serbia	RS	31	67.74	MS	13	62.2	30.8	SOC	18	65.9	38.9
Farcy *et al*[11], 2022	United States	PS	321	60.12	MM	201	64.2	56.2	C/I	120	66.3	58.3
San Filippo *et al*[39], 2022	United States	RS	453	47.01	MM	183	66.9	44.8	C/I	270	63.4	51.9
Ganesh *et al*[27], 2021	United States	RS	4670	50.62	MM	2335	63	54.2	SOC	2335	63	55.1
Ganesh *et al*[28], 2021	United States	RS	3596	50.02	MM	2747	NA	53.3	C/I	849	NA	48.3
Gottlieb *et al*[29], 2021	United States	RCT	577	45.40	MM	309	NA	NR	PBO, B/E	156	NA	NA
Heller *et al*[31], 2023	Germany	RS	26	45	MM	10	81	NR	SOC, C/I	23	NA	NA
Iqbal *et al*[8], 2021	United States	RS	284	NA	MM	144	NR	10.3	SOC	140	NA	63.60
Karr *et al*[10], 2022	United States	RS	46	63.04	MM	40	69	65	SOC	6	69	50
Kumar *et al*[32], 2022	United States	RS	403	52.10	MM	218	66	50.5	SOC	185	62	43.8
ACTIV-3/TICO LY-CoV555 Study Group *et al*[30], 2021	United States	RCT	314	57.32	NA	163	63	72	PBO	151	59	65
McCreary *et al*[33], 2021	United States	RCT	1935	46.20	MM	128	57	47	B/E, C/I	1807	NA	NA
Monday *et al*[34], 2022	United States	RCT	643	42.76	MM	294	61	72.8	B/E	349	55	72.4
Murillo *et al*[35], 2022	United States	RS	107	42.99	MM	39	NA	NA	SOC	63	NA	NA
Priest *et al*[36], 2022	United States	RS	758	49	MM	379	NA	88	SOC	379	NA	88

Quenzer *et al*[37], 2022	United States	RS	270	51.85	MM	134	60.3	92.5	SOC	136	63.3	69.1
Rubin *et al*[38], 2021	United States	RS	1257	43.75	NA	191	64	NR	SOC	1066	64.6	NA
Savoldi *et al*[40], 2022	Italy	PS	635	61.57	MM	161	63	72.7	B/E, C/I	474	NR	NA
Sridhara *et al*[41], 2023	United States	RS	2182	42.98	NA	1099	64	52.8	SOC	1091	46	20.9
Voelker and Jerath[42], 2022	United States	PS	678	43.65	NA	380	NA	NA	C/I	298	NA	NA
Webb *et al*[43], 2021	United States	QES	13534	55.19	NA	479	65	90.8	SOC, C/I	5651	NA	NA

[1]The percentage of patients with at least one comorbidity.

B/E: Bamlanivimab/etesevimab; C/I: Casirivimab/imdevimab; QES: Quasi-experimental study; MM: Mild to moderate; MS: Mild to severe; MC: Mild to critical; mAb: Monoclonal antibody; N: Number; NA: Not acquired; PBO: Placebo; PS: Prospective study; RCT: Randomized clinical trial; RS: Retrospective study; SOC: Standard of care.

significant difference was detected between the hospitalization rate of the bamlanivimab group compared to mAbs one (RR = 1.44; 95%CI: 1.07-1.94, P = 01, I^2 = 53%) (Supplementary Figure 2).

ED visits: The combined analysis of these studies revealed a significant difference in the frequency of ED visits between bamlanivimab-treated patients and those receiving SOC (RR = 0.69; 95%CI: 0.47-0.99, P = 0.04, I^2 = 58%). No significant difference was observed between bamlanivimab and other mAbs in terms of ED visits (RR = 0.96; 95%CI: 0.76-1.20, P = 0.74, I^2 = 0%) (Figure 2C and Supplementary Figure 3).

ICU admission: The result of meta-analysis showed no significant difference in the ICU admission rate of the bamlanivimab-treated patients and those receiving SOC (RR = 0.82; 95%CI: 0.57-1.18, P = 0.29, I^2 = 42%) (Figure 2D). No significant difference was observed between bamlanivimab and other mAbs in terms of ICU admission (RR = 1.60; 95%CI: 0.86-2.98, P = 0.13, I^2 = 0%) (Supplementary Figure 4).

Safety outcomes

Any adverse events: The pooled estimate of included studies showed no significant difference in adverse events between the bamlanivimab and SOC/PBO groups (RR = 1.01; 95%CI: 0.81-1.26, P = 0.88, I^2 = 0%) (Figure 2E). Moreover, no significant difference was observed in adverse events between the bamlanivimab and other mAb groups (RR = 6.13; 95%CI: 0.71-52.72, P = 0.09, I^2 = 1%) (Supplementary Figure 5).

Publication bias: No evidence of publication bias was detected for pooled estimate of mortality rate (P = 0.24) and hospitalization rate (P = 0.11) based on Begg test. However, Egger's test indicated a publication bias for pooled estimates of mortality rate (P = 0.01) and hospitalization rate (P = 0.004) (Supplementary Figures 6 and 7).

Subgroup and sensitivity analyses: The subgroup analysis showed no significance difference in mortality rate and hospitalization rate by mean age of patients treated with bamlanivimab compared to SOC/PBO and by sample size (Table 2). Sensitivity analysis also exhibited no significant change compared to the excluded studies (Table 2).

Table 2 Subgroup and sensitivity analyses for efficacy and safety outcomes

Analysis	Studies, *n*	Sample size, *n*	Point estimate (95%CI)	*P* value	Heterogeneity		
					Q value	*P* value	I^2
Sensitivity analysis							
Mortality rate soc (excluding Brock 2021and Djuric 2021)	16	29091	0.52 (0.37-0.73)	< 0.001	18.45	0.24	18.71
Hospitalization rate (excluding Brock 2021)	17	26565	0.55 (0.42-0.71)	< 0.001	69.65	0.21	77.02
Hospitalization rate (excluding Voelker 2022)	7	8177	1.38 (1.00-1.92)	0.04	14.25	0.02	57.91
ICU admission (excluding Brock 2021)	6	15759	0.88 (0.60-1.29)	0.52	7.79	0.16	35.81
Subgroup analysis							
Hospitalization rate by design, BAM *vs* SOC/PBO							
OS	16	25904	0.67 (0.60-0.75)	< 0.001	82.27	< 0.001	81.76
RCT	2	769	0.44 (0.21-0.94)	0.03	1.95	0.16	48.80
Hospitalization rate by sample size, BAM *vs* SOC/PBO							
< 1000	11	23453	0.51 (0.43-0.61)	< 0.001	50.51	< 0.001	80.20
≥ 1000	7	3220	0.77 (0.67-0.89)	< 0.001	22.22	0.001	73.00
Hospitalization rate by mean age, BAM *vs* SOC/PBO							
< 65	8	22783	0.77 (0.67-0.88)	< 0.001	26.91	< 0.001	73.99
≥ 65	4	1918	0.46 (0.32-0.66)	< 0.001	0.30	0.96	< 0.001
Mortality rate by design, BAM *vs* SOC/PBO							
OS	17	28916	0.44 (0.31-0.62)	< 0.001	14.67	0.54	0.00
RCT	1	314	1.67 (0.57-4.86)	0.34	0.00	1.00	0.00
Mortality rate by sample size, BAM *vs* SOC/PBO							
< 1000	12	4030	0.48 (0.31-0.76)	0.002	15.55	0.15	29.29
≥ 1000	6	25200	0.51 (0.31-0.84)	0.009	4.43	0.48	0.00
Mortality rate by mean age, BAM *vs* SOC/PBO							
< 65	8	25639	0.60 (0.37-0.96)	0.037	9.89	0.19	29.26
≥ 65	5	2189	0.40 (0.20-0.79)	0.008	5.16	0.27	22.53

CI: Confidence interval; ED: Emergency department; mAb: Monoclonal antibody; PBO: Placebo; RCT: Randomized clinical trial; OS: Observational study; SOC: Standard of care.

DISCUSSION

The objective of this study was to analyze and synthesize the most recent evidence on the effectiveness and safety of bamlanivimab, a mAb intervention, during the prevalence of the SARS-CoV-2 Omicron variant. Despite the protective role of vaccines against SARS-CoV-2 infection, effective treatments are still required to manage COVID-19 disease, particularly with the emergence of new variants[44]. The results demonstrated the efficacy of bamlanivimab in achieving positive clinical outcomes among patients diagnosed with COVID-19.

The results of the meta-analysis revealed a significantly lower mortality rate in the bamlanivimab-receiving individuals compared to those treated with SOC/PBO. However, this difference was not significant between the bamlanivimab and other mAb groups. Clinical studies showed the similar efficacy of mAb treatments in reducing COVID-19-induced death [11,40]. Consistent to our findings, meta-analyses conducted on the efficacy of bamlanivimab revealed that treatment with bamlanivimab is significantly associated with a lower mortality rate compared to the control group[45,46]. In general, the clinical evidence suggests that mAb treatments may contribute to a reduction in the mortality rate among patients with COVID-19[4,30,34,42,47]. Targeting the spike protein of the SARS-CoV-2 virus with anti-SARS-CoV-2 mAbs may serve as a potential mechanism for reducing the mortality rate of COVID-19 patients[48].

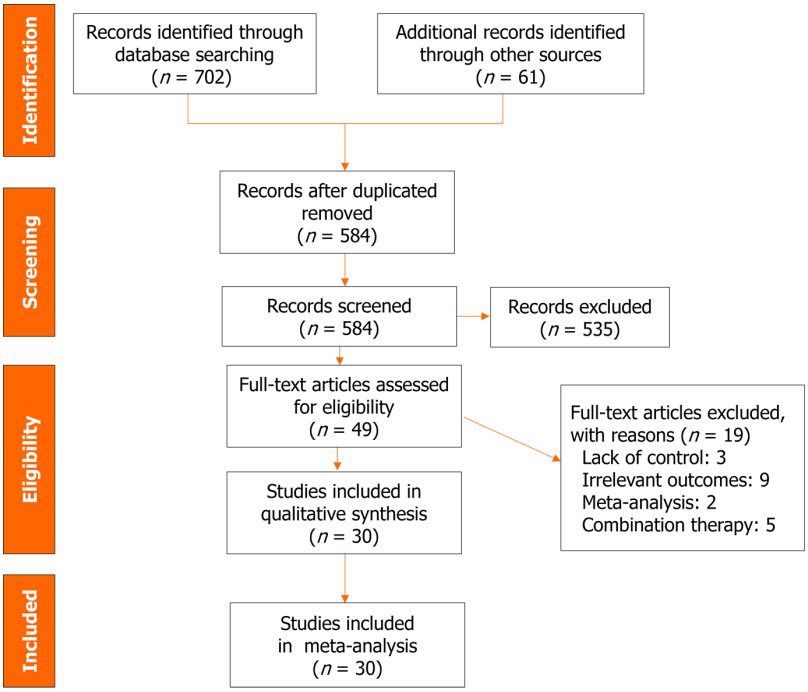


Figure 1 PRISMA flow diagram of study selection process.

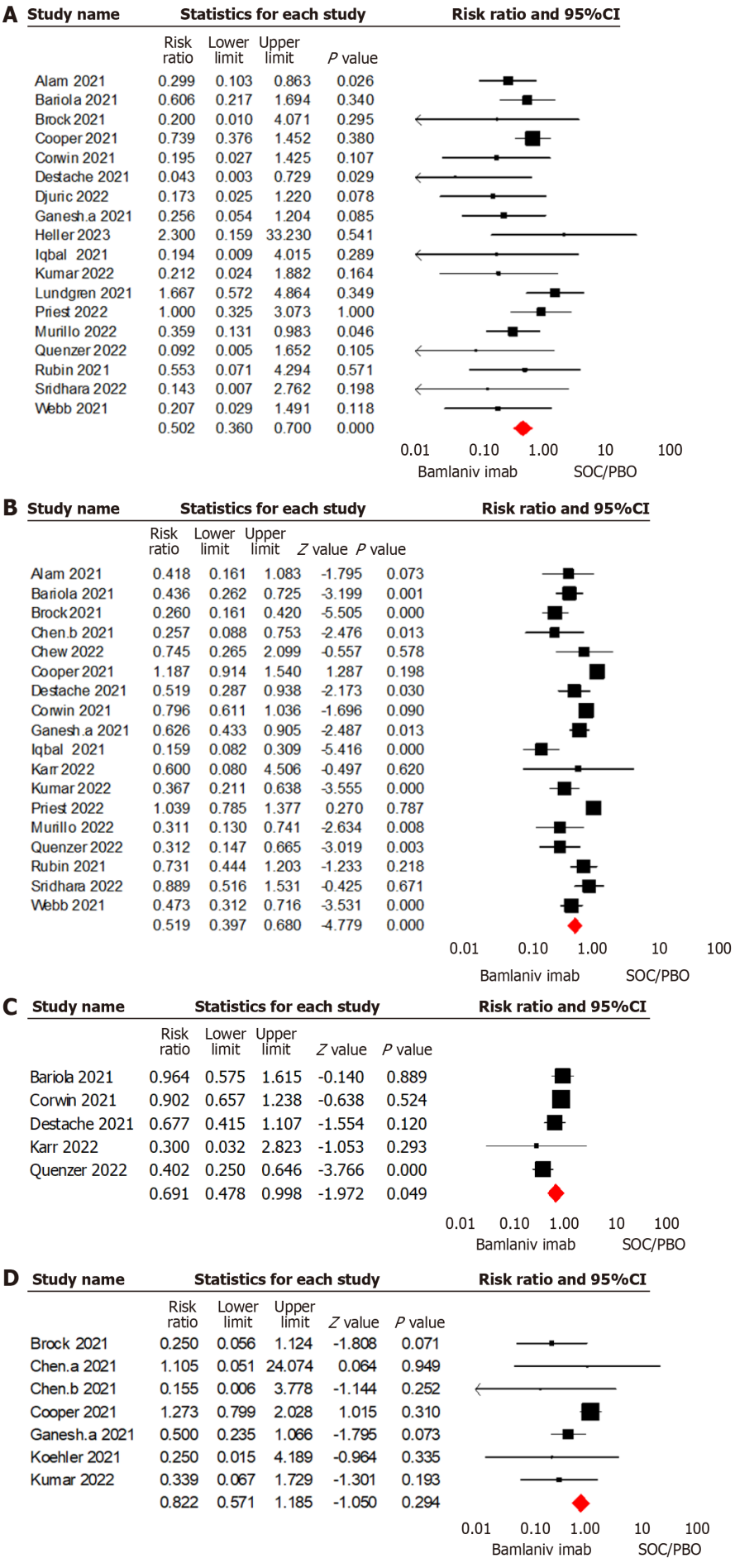
According to results of the present meta-analysis, bamlanivimab-treated patients had a lower likelihood of being admitted to the hospital compared to those receiving SOC/PBO. However, hospitalization rate was higher in the bamlanivimab group than the other mAbs group. Bamlanivimab treatment may contribute to a reduced rate of hospitalization among COVID-19 patients. Consistent with the mentioned finding, other meta-analyses[45,46] on the efficacy of this drug also demonstrated that treatment with bamlanivimab is associated with a lower rate of hospitalization in patients with mild to moderate COVID-19 compared to control groups. This further supports the potential effectiveness of bamlanivimab in reducing the hospital admission in individuals with COVID-19. Indeed, real-world studies demonstrated that therapeutic mAbs, including bamlanivimab[38,40], sotrovimab, casirivimab/imdevimab[4,40], and bamlanivimab/etesevimab[40] can significantly reduce the rate of COVID-19-related hospitalization. According to these studies, the use of these mAbs can effectively lower the severity of the disease and decrease the need for hospitalization in individuals affected by COVID-19.

The results of the present study demonstrate a significant positive effect of bamlanivimab on reducing the need for ED visits in patients with COVID-19 compared to SOC/PBO. However, this difference was not significant between the bamlanivimab and other mAb groups. A meta-analysis of RCTs comparing mAbs-receiving patients with PBO group indicated a significant association of mAbs with a lower rate of ED visits[49]. A possible explanation for this difference could be due to differences in the type of mAb treatments as intervention or included in the study design.

According to the present meta-analysis, treatment with bamlanivimab was not significantly associated with a lower rate of admission to ICU compared to SOC/PBO or mAbs. On the contrary, a meta-analysis by Xiang *et al*[45] showed a significant association of bamlanivimab with reduced ICU admission rate compared to the controls. This difference can be due to the number of studies included in the quantitative analysis. Compared to Xiang *et al*[45], the present research identified and included more studies in the meta-analysis of data on ICU admission rate.

Consistent with previously published meta-analyses[45] on the safety profile of bamlanivimab, the present study found similar incidence of adverse events in both the bamlanivimab and control groups. In general, the bamlanivimab-related incidence of adverse events in COVID-19 patients was mild and well-tolerated[11,19,39]. The most frequent adverse events in studies included nausea, diarrhea, headache, and respiratory distress[21,29]. In terms of severe adverse events, no significant difference was observed between the bamlanivimab and control groups. Chen *et al*[21] found no cases of discontinuations due to adverse events in bamlanivimab-treated patients at different doses (700, 2800, and 7000 mg). Gottlieb *et al*[29] also found similar results in COVID-19 patients receiving bamlanivimab doses of 700, 2800, and 7000 mg.

Two important points should be considered in the interpretation of the present results. First, several studies have documented evidence of post-COVID-19 condition among individuals after the initial SARS-CoV-2 infection which is a serious problem for many recovered COVID-19 patients[50-52]. Given the importance of post-COVID-19 conditions in designing effective treatments for COVID-19, and considering the lack of validated treatment for these conditions, it is crucial to conduct longitudinal monitoring of COVID-19 patients. This monitoring is vital for the development of effective therapeutic agents[52]. Second, studies have shown the resistance of some SARS-COV-2 variants to bamlanivimab. Hoffmann *et al*[53] reported the resistance of SARS-CoV-2 variant B.1.1.7 to bamlanivimab. A study conducted by Peiffer-Smadja *et al*[54] showed the emergence of resistance mutants in bamlanivimab-receiving COVID-19 patients. A RCT conducted by Choudhary *et al*[55] reported the emergence of SARS-CoV-2 escape mutations in COVID-19 patients during


A
Study name
Statistics for each study
Risk ratio and 95%CI
Risk ratio
Lower limit
Upper limit
P value
Alam 2021 0.299 0.103 0.863 0.026
Bariola 2021 0.606 0.217 1.694 0.340
Brock 2021 0.200 0.010 4.071 0.295
Cooper 2021 0.739 0.376 1.452 0.380
Corwin 2021 0.195 0.027 1.425 0.107
Destache 2021 0.043 0.003 0.729 0.029
Djuric 2022 0.173 0.025 1.220 0.078
Ganesh.a 2021 0.256 0.054 1.204 0.085
Heller 2023 2.300 0.159 33.230 0.541
Iqbal 2021 0.194 0.009 4.015 0.289
Kumar 2022 0.212 0.024 1.882 0.164
Lundgren 2021 1.667 0.572 4.864 0.349
Priest 2022 1.000 0.325 3.073 1.000
Murillo 2022 0.359 0.131 0.983 0.046
Quenzer 2022 0.092 0.005 1.652 0.105
Rubin 2021 0.553 0.071 4.294 0.571
Sridhara 2022 0.143 0.007 2.762 0.198
Webb 2021 0.207 0.029 1.491 0.118
0.502 0.360 0.700 0.000
0.01 0.10 1.00 10 100
Bamlaniv imab SOC/PBO
B
Study name
Statistics for each study
Risk ratio and 95%CI
Risk ratio
Lower limit
Upper limit
Z value
P value
Alam 2021 0.418 0.161 1.083 -1.795 0.073
Bariola 2021 0.436 0.262 0.725 -3.199 0.001
Brock 2021 0.260 0.161 0.420 -5.505 0.000
Chen.b 2021 0.257 0.088 0.753 -2.476 0.013
Chew 2022 0.745 0.265 2.099 -0.557 0.578
Cooper 2021 1.187 0.914 1.540 1.287 0.198
Destache 2021 0.519 0.287 0.938 -2.173 0.030
Corwin 2021 0.796 0.611 1.036 -1.696 0.090
Ganesh.a 2021 0.626 0.433 0.905 -2.487 0.013
Iqbal 2021 0.159 0.082 0.309 -5.416 0.000
Karr 2022 0.600 0.080 4.506 -0.497 0.620
Kumar 2022 0.367 0.211 0.638 -3.555 0.000
Priest 2022 1.039 0.785 1.377 0.270 0.787
Murillo 2022 0.311 0.130 0.741 -2.634 0.008
Quenzer 2022 0.312 0.147 0.665 -3.019 0.003
Rubin 2021 0.731 0.444 1.203 -1.233 0.218
Sridhara 2022 0.889 0.516 1.531 -0.425 0.671
Webb 2021 0.473 0.312 0.716 -3.531 0.000
0.519 0.397 0.680 -4.779 0.000
0.01 0.10 1.00 10 100
Bamlaniv imab SOC/PBO
C
Study name
Statistics for each study
Risk ratio and 95%CI
Risk ratio
Lower limit
Upper limit
Z value
P value
Bariola 2021 0.964 0.575 1.615 -0.140 0.889
Corwin 2021 0.902 0.657 1.238 -0.638 0.524
Destache 2021 0.677 0.415 1.107 -1.554 0.120
Karr 2022 0.300 0.032 2.823 -1.053 0.293
Quenzer 2022 0.402 0.250 0.646 -3.766 0.000
0.691 0.478 0.998 -1.972 0.049
0.01 0.10 1.00 10 100
Bamlaniv imab SOC/PBO
D
Study name
Statistics for each study
Risk ratio and 95%CI
Risk ratio
Lower limit
Upper limit
Z value
P value
Brock 2021 0.250 0.056 1.124 -1.808 0.071
Chen.a 2021 1.105 0.051 24.074 0.064 0.949
Chen.b 2021 0.155 0.006 3.778 -1.144 0.252
Cooper 2021 1.273 0.799 2.028 1.015 0.310
Ganesh.a 2021 0.500 0.235 1.066 -1.795 0.073
Koehler 2021 0.250 0.015 4.189 -0.964 0.335
Kumar 2022 0.339 0.067 1.729 -1.301 0.193
0.822 0.571 1.185 -1.050 0.294
0.01 0.10 1.00 10 100
Bamlaniv imab SOC/PBO

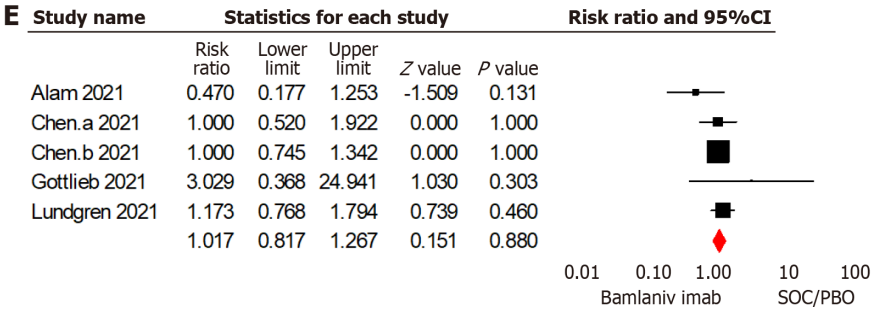


Figure 2 Forest plot analysis. A: Forest plot analysis for the outcome of mortality rate of bamlanivimab *vs* standard of care/placebo (SOC/PBO) in patients with coronavirus disease 2019 (COVID-19); B: Forest plot analysis for the outcome of hospitalization rate of bamlanivimab *vs* SOC/PBO in patients with COVID-19; C: Forest plot analysis for the outcome of emergency department visit of bamlanivimab *vs* SOC/PBO in patients with COVID-19; D: Forest plot analysis for the outcome of intensive care unit admission of bamlanivimab *vs* SOC/PBO in patients with COVID-19; E: Forest plot analysis for the outcome of adverse events of bamlanivimab *vs* SOC/PBO in patients with COVID-19. CI: Confidence interval.

treatment with bamlanivimab (700 mg). However, no resistance mutations were identified in patients treated with 7000 mg bamlanivimab. These findings highlight the importance of viral resistance during the development of treatments for COVID-19 patients. SARS-CoV-2 mutations may also lower the effectiveness of current preventive therapies in individuals, including vaccines. The SARS-CoV-2 variant B.1.351 could significantly reduce the efficacy of Novavax COVID-19 vaccine[56].

The present study has some remarkable limitations. Firstly, the included studies did not report the type of SARS-CoV-2 variant. Therefore, the present findings may not be applicable to some SARS-COV-2 variants of interest. Secondly, the majority of studies included in the meta-analysis were retrospective, causing an inherent risk of bias. Moreover, many of these retrospective studies did not utilize propensity score matching to minimize selection bias and confounding variables. Thirdly, we could not perform subgroup analyses based on these variables as the information on the comorbidity percentage and COVID-19 vaccine status of the studies was not complete. Therefore, the present results cannot be generalized to patients with unknown COVID-19 vaccine status. Finally, the present results should be interpreted with caution due to the presence of potential publication bias in several outcomes.

CONCLUSION

The present meta-analysis demonstrated the association of bamlanivimab treatment with a reduction in the mortality rate, hospitalization rate, and ED visits in patients with COVID-19 compared to SOC-receiving group. However, it did not show a significant efficacy in improving clinical outcomes compared to other mAb treatments. In terms of safety, bamlanivimab was safe and well-tolerated in patients with COVID-19. However, studies did not report the specific type of SARS-CoV-2 variants. Therefore, the findings may not be directly applicable to patients with current SARS-CoV-2 variants. Future research should be focused on the efficacy of bamlanivimab against the current SARS-CoV-2 variants, especially in immunocompromised patients who are more susceptible to the new SARS-CoV-2 variants in terms of mutations and resistance to treatment with mAbs. Moreover, the comorbidity percentage and COVID-19 vaccination rate should be considered in evaluating the efficacy of bamlanivimab in COVID-19 patients.

ARTICLE HIGHLIGHTS

Research background

Bamlanivimab, a monoclonal antibody (mAb), has been used as a therapeutic agent for patients with coronavirus disease 2019 (COVID-19). Previous studies have shown that bamlanivimab may be effective in treating COVID-19 patients.

Research motivation

Despite several studies evaluating the clinical benefit of bamlanivimab in COVID-19 patients, there is currently no comprehensive systematic review and meta-analysis assessing its efficacy and safety as a treatment.

Research objectives

This study aims to evaluate the use of bamlanivimab in improving efficacy outcomes compared to other treatments in COVID-19 patients. Additionally, the safety profile of bamlanivimab is compared to control groups.

Research methods

A thorough search was conducted in PubMed, Cochrane Library, Web of Science, medRxiv, and Google Scholar up to January 25, 2023. Cochrane bias tools were utilized to assess the risk of bias in the included studies. Data analysis was

performed using Comprehensive Meta-Analysis software (version 3).

Research results

A total of 30 studies were identified and included in the meta-analysis. The meta-analysis revealed a significant difference between the bamlanivimab and standard of care/placebo groups in terms of mortality rate, hospitalization rate, and emergency department (ED) visits. However, there was no significant difference between the two groups regarding intensive care unit (ICU) admission. When compared to other mAbs, bamlanivimab did not demonstrate superior efficacy in terms of hospitalization rate, mortality rate, ICU admission, and ED visits. No significant difference was observed between the treatment groups in terms of adverse events.

Research conclusions

Although the present results demonstrate the efficacy and safety of bamlanivimab in treating COVID-19, further research is necessary to confirm its effectiveness against novel circulating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants.

Research perspectives

In the future, studies should be focused on the efficacy of bamlanivimab against the current SARS-CoV-2 variants, especially in immunocompromised patients who are more susceptible to the new SARS-CoV-2 variants in terms of mutations and resistance to treatment with mAbs. Moreover, the comorbidity percentage and COVID-19 vaccination rate should be considered in evaluating the efficacy of bamlanivimab in COVID-19 patients.

FOOTNOTES

Author contributions: Amani B designed and administrated the study, and drafted the manuscript; Khodavirdilou L and Kardan Moghaddam V carried out the literature search; Kardan Moghaddam V and Akbarzadeh A performed the data extraction; Rajabkhah K and Kardan Moghaddam V were involved in assessing the quality of studies; Amani B and Akbarzadeh A performed the data analysis; Amani B and Khodavirdilou L performed the writing, review & editing; and all authors have read and approved the final manuscript.

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P-Editor: Zhao S

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