Original Article

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Comparison of Monoclonal Antibody Cocktail (Casirivimab-Imdevimab) Treatment with Remdesivir and Favipiravir in Mild to Moderate COVID-19 Infection: A Retrospective Study

Internal Medicine Section

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ABSTRACT

Introduction: Favipiravir and remdesivir are antiviral drugs being used in the COVID pandemic and were also used previously for other viral infections in the past. Monoclonal antibody (Mab) Casirivimab-Imdevimab is a Coronavirus Disease 2019 neutralising antibody approved in the last one year. Therefore, a clinical comparison with the existing treatment modalities is imperative.

Aim: To compare Mab with remdesivir and favipiravir for mild to moderate COVID-19 disease.

Materials and Methods: A retrospective, observational and single-centre study was conducted at a COVID-19 infection facility and private tertiary care hospital, Mumbai, Maharashtra, India. Data of patients admitted during the period of 1st June 2021 to 31st August 2021 was collected and analysed in the months of September 2021 and October 2021. Adults participants diagnosed to have COVID-19 infection, not requiring critical care or oxygen therapy were included in the study. Time to recovery from treatment onset and the need for treatment escalation were the primary outcome measures. Data was entered into Microsoft excel spreadsheet version 16 and analysed. Statistical analysis was carried out using Chi-square test for the significance of association between tabulated values of data for qualitative and categorical data. Two-tailed unpaired t-test and Analysis of Variance (ANOVA) was used for quantitative tabulated data.

Results: This study included 158 participants, grouped into remdesivir (n=63), favipiravir (n=30) and Mab (n=65) treatment groups. Gender distribution was comparable in all groups (p-value=0.08). The three groups were compared for need of treatment escalation and time of recovery. The Mab treatment group (on comparing with other treatment arms) had earlier symptom recovery when given to patients with mild COVID-19 disease (p-value=0.006 for major symptoms) or when treatment was started within five days of symptom onset (p-value <0.001). Patients in Mab treatment group with mild illness required no treatment escalation compared to other groups (p-value=0.011). However, time to recovery patients in all treatment groups was comparable in case of patients with moderate COVID-19 illness (p-value=0.7381). In patients with moderate COVID-19 illness Mab treatment group required more frequent treatment escalation compared to remdesivir treatment group (p-value=0.044), when treatment was started within 5 days of symptom onset remdesivir and mab were comparable for treatment escalation (p-value=0.144). Vaccination status of the three groups differed significantly (p-value=0.033) hence a further subanalysis was done. On further analysis, non vaccinated patients receiving Mab recovered from minor symptoms (p-value=0.0006) earlier than those receiving Remdesivir. Amongst the participants of the Mab treatment-group, vaccinated and non-vaccinated patients had comparable recovery time and need for treatment escalation (p-value=0.57 and p-value=0.76, respectively). Participants who received Mab-treatment within five days of symptom onset; recovered earlier compared to those who received Mab treatment after five days (p-value=0.019).

Conclusion: Monoclonal antibody treatment group compared to the other treatment groups had earlier recovery in non vaccinated patients, mild COVID-19 disease, and when treatment was started before or on the 5th day of symptom onset.

Keywords: Antiviral, Coronavirus disease 2019, Recovered, Vaccination

INTRODUCTION

Since the onset of the Coronavirus Disease 2019 (COVID-19) pandemic, several treatment modalities have been tried [1,2]. Drugs like remdesivir continue to be in use [2,3]. Whereas, other treatment modalities namely ivermectin and hydroxychloroquine were withdrawn [3]. Various antibody treatments have been introduced, such as the two novel antibody (nAb) cocktails {Casirivimab-Imdevimab Monoclonal antibody (Mab) cocktail and Bamlanivimab-Etesevimab} and one nAb monotherapy (Bamlanivimab) [4]. These treatment modalities have been granted Emergency Use Authorisation (EUA) by the United States (US) Food and Drug Administration (FDA) and the European Medicines Agency for the treatment of ambulatory patients who have a high-risk of progressing to severe disease [3,4]. As Mab is a neutralising therapy, the efficacy of Mab in patients with severe COVID-19 patients have been varied [4,5]. However, early data suggest a promising role for nAbs/Mab in preventing COVID-19 progression, and hence it has been incorporated in the Infectious Diseases Society of America (IDSA) guidelines for susceptible variants [3]. The Monoclonal antibody (Mab) cocktail is suggested to prevent disease progression and reduce morbidity and mortality [4,5].

Recent clinical data have demonstrated the clinical activity of remdesivir in terms of faster time to recovery in patients with severe COVID-19 and higher Odd's ratio of improved clinical status in patients with moderate COVID-19 [6]. Remdesivir is approved by IDSA for mild to moderate disease patients, who are at risk of progression to severe disease [7]. Favipiravir, an antiviral drug has been used for treating COVID-19 in several countries including Japan, Russia, China and India, under emergency provisions for the initial wave of COVID-19 [8,9,10,11].

As remdesivir and favipiravir are two common drugs used in the country for COVID-19 illness [11,12]; this study aimed to compare the effect of remdesivir and favipiravir with that of Mab treatment in terms of mortality, recovery time from onset of treatment, and progression to severe or critical disease.

MATERIALS AND METHODS

The present retrospective, observational and single-centre study was conducted at a COVID-19 infection facility, Dr. Balabhai Nanavati Hospital, a tertiary care hospital in Mumbai, Maharashtra, India. Data of patients admitted to the facility from 1st June 2021 to 31st August 2021 was accessed from institutional medical records from September 2021 to October 2021, after procuring ethical clearance from Institutional Ethical Committee (IEC No: BNH/90/2021).

Inclusion criteria: Adults (18 years and above) with mild to moderate COVID-19 disease with laboratory confirmed (Real time-polymerase chain reaction or rapid antigen test) COVID-19 infection, not requiring oxygen therapy at the time of admission were included in the study.

Exclusion criteria: Patients having an interval of more than 10 days between the onset of symptoms and onset of treatment and pregnant females were excluded from the study.

Study Procedure

The data was divided into three groups based on the choice of treatment given (remdesivir, Mab and favipiravir). Each group included mild and moderate severity patients. Subanalysis for each severity was done separately. Treatment choice was decided by the treating physician and the patient. Patients receiving Mab were admitted in the Inpatient Department for logistic reasons. As per state [11] and central government [12] treatment guidelines, favipiravir was used for mild to moderate cases until 10 days of symptom onset for those at low risk of progression to severe disease. Remdesivir was reserved for moderate severity COVID-19 illness as per guidelines [11]. However, at the institutional level it was also used for mild patients with high-risk of progression to severe disease. Mab was introduced at the institutional level on 1st June 2021. As per international guidelines (IDSA) it was reserved for patients with mild to moderate severity COVID-19 with high-risk of progression to severe disease [7]. As the cost of Mab was high, it was a factor that influenced the selection of treatment choice for patients.

Mortality, time to recovery from symptoms (absence of symptoms), and delayed recovery or worsening (reported through the need for treatment escalation) were the primary outcomes. Patients were defined as mild or moderate COVID-19 disease as per National Institute of Health guidelines [13].

For purposes of statistical analysis, patients in each treatment group were classified as those having mild symptoms and those having moderate symptoms (patients with severe symptoms were not included in the study). Cough, fever, breathlessness was counted as major symptoms. Malaise and weakness that lingered on for many days for a few patients were considered minor symptoms. Variables that were further evaluated included time to treatment from symptom onset (≤5 days vs >5 days) and status of vaccination (fully vaccinated vs not vaccinated).

Patients were defined as vaccinated, when vaccinated with two doses as per regional guidelines with either Covishield® (adenovirus ChAdOx1) or Covaxin® (BBV152) COVID-19 vaccines [14]. Vaccination status was taken into consideration only when 15 days had elapsed after the last dose of vaccination [15]. A separate analysis was done for patients who had completed two doses of COVID-19 vaccination.

Missing data: Initially there were 64 participants in remdesivir group and 66 in Mab group. One patient from the remdesivir and Mab group, each was excluded due to insufficient data, making it 63 in remdesivir group and 65 in Mab group.

Sample size calculation: Alpha error was considered to be 0.05%, Power of the study was taken as 80%. As no previous data was available for comparison between remdesivir, favipiravir, and Mab, a pilot study was conducted, and mean values of time to recovery for symptom resolution from treatment onset for remdesivir and Mab treatment group, from the study were taken (Mean time to recovery from symptoms for Mab group with 10 patients 3±2.89, mean for remdesivir 5.3±3.13). The sample size was hence calculated as 25 minimum in each group [16].

STATISTICAL ANALYSIS

Data were recorded and tabulated in Microsoft excel spreadsheet version 16. Chi-square test was used to test the significance of association between tabulated values of data and qualitative, categorical data [17]. Two-Tailed unpaired t-test and ANOVA analyses were used to compare differences between the mean of quantitative measurements [18,19]. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

The present retrospective study comprised a total of 158 participants. Data were grouped into three treatment groups; i.e. remdesivir (n=63), favipiravir (n=30) and Mab (n=65) treatment group. Gender distribution was comparable in all groups (p-value=0.08). Remdesivir group had more moderate severity patients and Mab treatment group had more mild severity COVID-19 patients when compared with other treatment groups (p-value <0.001). Patients of Mab treatment group were significantly older (p-value <0.0001) with more co-morbidities and favipiravir treatment group had younger participants [Table/Fig-1]. All groups were comparable for major symptom distribution (p-value=0.062).

Pretreatment analysis		Remdesivir, n=63	Favipiravir, n=30	Mab, n=65	p-value
Age (years) (Mean±SD)		53.89±16.62	48.36±18.58	63.71±13.29	<0.000001‡
Gender	Female	37	11	39	0.08
	Male	26	19	26	
Severity	Mild	7	17	37	<0.001‡
	Moderate	56	13	28	
Average lag of days between symptom onset and treatment onset (Mean±SD)		5.31±2.21	3.96±2.62	3.73±2.3	0.0001‡
Major symptoms		61	27	55	0.0619
Minor symptoms		63	30	61	-
Vaccination status analysis					
Vaccinated with two doses of COVID-19 vaccine†		13	9	33	0.0014‡ (By ANOVA analysis- comparison of unvaccinated with two doses vs one dose of vaccine taken) 0.033‡ (Vaccinated with two doses vs not vaccinated)
Vaccinated with one dose of COVID-19 vaccine		19	8	5	
Not vaccinated history		31	13	27	
History of COVID-19 infection		1	1	0	N.A.*

Co-morbidities in participants				
Malignancy	0	1	1	N.A.*
Diabetes mellitus	19	7	30	0.06
Hypertension	26	9	39	0.016‡
BA	0	1	1	N.A.*
IHD	8	1	10	0.267

[Table/Fig-1]: Depicting baseline characteristic and co-morbidities of the study participants.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019; *: Values too small to analyse; †Bonferroni test applied; ‡p-value <0.05 was considered statistically significant

Mab treatment group recovered earlier when compared to other groups for major symptoms (p-value=0.0011). The number of patients requiring treatment escalation was higher in the favipiravir group when compared to the Mab and remdesivir groups (p-value=0.005). Prevalence of secondary infection during treatment for COVID-19 illness was comparable in all three groups (p-value=0.455) [Table/Fig-2].

Mab group had a statistically significant shorter time to recovery when treatment was started ≤5 days after symptoms onset (p-value <0.002). Favipiravir required a more frequent escalation of treatment compared to the other two groups when treatment was initiated on the 5th day from symptom onset or before (p-value=0.0033) [Table/Fig-3].

Parameters	Remdesivir, n=63	Favipiravir, n=30	Mab, n=65	p-value
The duration between treatment onset and symptom resolution for major symptoms (Mean±SD)	5.19±2.20	4.76±2.48	3.59±2.66	0.0011*
The duration between treatment onset and symptom resolution for minor symptoms (Mean±SD)	5.98±2.53	6.4±2.28	4.30±3.91	0.02† (Mab vs Remdesivir, p-value=0.007)
Need for escalation of COVID-19 treatment	9	14	10	0.005† (comparable for Mab vs Remdesivir)
Secondary infection	3	1	6	0.455
Mortality	0	0	2	-

[Table/Fig-2]: Post-treatment analysis of study participants depicting symptom recovery time and need for treatment escalation.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019.†Bonferroni test applied; *p-value <0.05 was considered statistically significant

Analysis for patients who had COVID-19 disease					
(a) Analysis for patients who received treatment within 5 days from symptom onset		**Remdesivir, n=31**	**Favipiravir, n=21**	**Mab, n=49**	**p-value**
Average lag of days between symptom onset and treatment onset (Mean±SD)		3.52±1.36	2.52±1.36	2.73±1.60	0.028*
COVID-19 severity	Mild	5	14	35	<0.00001*
	Moderate	26	7	14	
The duration between treatment onset and symptom resolution for major symptoms (Mean±SD)		5.16±1.63	4.78±2.12	3.13±2.39	0.002*
The duration between treatment onset and symptom resolution for minor symptoms (Mean±SD)		5.77±1.7	6.42±1.99	3.71±3.24	0.0001*
Need for escalation of COVID-19 treatment		4	9	5	0.0033† (on comparing Mab with Remdesivir; p=0.7)
(b) Analysis for mild COVID-19 patients		**Remdesivir, n=7**	**Favipiravir, n=17**	**Mab, n=37**	**p-value**
Average lag of days between symptom onset and treatment (Mean±SD)		5.14±2.67	3.58±2.78	2.78±1.76	0.032*
The duration between treatment onset and symptom resolution for major symptoms (Mean±SD)		5.85±1.57	3.78±2.15	2.81±2.4	0.006*
The duration between treatment onset and symptom resolution for minor symptoms (Mean±SD)		6±1.63	5.47±2.21	3.38±3.75	0.033*
Need for escalation of COVID-19 treatment		1	4	0	0.011*
Analysis for mild COVID-19 patients with treatment onset ≤5th day of symptom		**Remdesivir, n=5**	**Favipiravir, n=14**	**Mab, n=35**	**p-value**
Average lag of days between symptom onset and treatment (Mean±SD)		3.8±1.64	2.42±1.1	2.57±1.56	0.18
The duration between treatment onset and symptom resolution for major symptoms such as fever cough and breathlessness (Mean±SD)		6.4±1.5	4.25±1.95	2.37±1.56	<0.001*
The duration between treatment onset and symptom resolution for minor symptoms (Mean±SD)		6.6±1.51	6±1.92	2.71±2.1	<0.001*
Need for escalation of covid treatment: requirement of oxygen or alternative treatment?		0	3	0	Not computable

[Table/Fig-3]: Analysis for patients who had COVID-19 disease.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019; †: Bonferroni test applied; *p-value <0.05 was considered statistically significant; The first p-value is a result of ANOVA analysis between all the three groups. Second p-value is specific for what is mentioned as those values were very close. For example, in the row 'Need for escalation of COVID-19 treatment' 0.0033 is p-value as per the Chi-square. Further Chi-square test was done for Mab vs remdesivir as favipirvair was clearly higher than those two and Mab vs remdesivir values are closer to each other numerically, hence the second p-value

In the subgroup of patients with mild symptoms: Overall time to recovery was statistically better in the Mab group compared to the favipiravir and remdesivir groups (p-value=0.006). The number of patients requiring treatment escalation was higher in the favipiravir group. Compared to the Mab group, remdesivir groups had more requirement of treatment escalation (p-value=0.011).

Further analysis was done for mild COVID-19 subgroup for patients whose treatment was initiated ≤5th day of symptom onset. The lag between symptom onset and treatment onset was comparable in all three groups (p-value=0.18). Participants of Mab group recovered earlier than those of remdesivir and favipiravir group (Major symptoms: p-value <0.001, Minor symptoms p-value=00.014). Favipiravir required more frequent treatment escalation (p-value=0.011), whereas no participant of Mab and remdesivir required any escalation of treatment [Table/Fig-3].

In the subgroup of patients with moderate symptoms: Overall time of recovery was the same in all three treatment groups (Major symptoms, p-value=0.738, Minor symptoms, p-value=0.075, [Table/Fig-4a], and this was not affected when the treatment was started earlier i.e., ≤5 days (major symptoms, p-value=0.59, minor symptoms, p-value=0.47, [Table/Fig-4b].

Compared to remdesivir treatment group, Mab and favipiravir treatment group required more frequent treatment escalation (p-value=0.007), [Table/Fig-4]. In moderate subgroup where treatment was initiated within 5 days of symptom onset escalation of treatment was less frequently required in remdesivir group. However, statistically requirement of escalation was comparable in Mab and remdesivir group but still significantly higher in favipiravir group (p-value=0.0017, [Table/Fig-4b]).

Subanalysis of the group Mab: No difference was found in vaccinated and non vaccinated patients of the Mab treatment group when compared for the need of treatment escalation and symptom recovery. Mab treatment group participants whose treatment started on the 5th day or before had earlier symptom recovery compared to Mab patients who received treatment later. Both groups were comparable for the need for escalation of treatment [Table/Fig-5].

Subanalysis of vaccinated vs non vaccinated participants: In the vaccinated subgroup, symptom recovery was comparable in all three treatment groups (p-value=0.199); however, treatment escalation was more likely to be needed in the favipiravir group compared to the other two groups (p-value=0.0017). In the non vaccinated subgroup, symptom recovery was earlier in the Mab-treatment group (Major symptoms: p-value=0.0001, Minor symptoms p-value=0.00016) [Table/Fig-6].

Parameters	Remdesivir, n=56	Favipiravir, n=13	Mab, n=28	p-value
Age in years (Mean±SD)	54.11±16.12	49.84±16.19	63.07±13.74	0.0154*
Average lag of days between symptom onset and treatment (Mean±SD)	5.38±2.18	4.54±2.26	5±2.35	0.44
The duration between treatment onset and symptom resolution for major symptoms such as fever cough and breathlessness (Mean±SD)	5.14±2.27	5.84±2.54	5.5±4.7	0.7381
The duration between treatment onset and symptom resolution for minor symptoms (Mean±SD)	5.98±2.642	7.61±1.61	5.53±3.86	0.075
Need for escalation of covid treatment: requirement of oxygen or alternative treatment?	8	7	9	0.007*, (p-value=0.044* for Mab vs remdesivir)

[Table/Fig-4a]: Analysis for patients with Moderate COVID-19 illness.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019; *p-value <0.05 was considered statistically significant

Parameters	Remdesivir, n=26	Favipiravir, n=7	Mab, n=14	p-value
Age in years (Mean±SD)	57.92±14.23	46±17.83	62.72±13.37	0.5953
Average lag of days between symptom onset and treatment (Mean±SD)	3.46±1.33	2.86±1.67	3.14±1.7	
The duration between treatment onset and symptom resolution for major symptoms such as fever cough and breathlessness (Mean±SD)	4.88±1.59	5.714±2.21	4.31±2.95	0.3771
The duration between treatment onset and symptom resolution for minor symptoms (Mean±SD)	5.6±1.57	7.28±1.97	5.57±4.13	1.1748
Need for escalation of covid treatment: requirement of oxygen alternative treatment?	4	6	5	0.0017*, (p-value=0.144 for Mab vs Remdesivir)

[Table/Fig-4b]: Analysis for patients with moderate COVID-19 illness with less than 5 days gap between symptom onset and treatment initiation.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019; *p-value <0.05 was considered statistically significant

Subanalysis for Mab treatment group			
(a) Analysing treatment response in COVID-19 vaccinated vs non vaccinated participants of the Mab treatment group	**Mab-vaccinated with 2 doses (n=33)**	**Mab-non-vaccinated (n=27)**	**p-value**
Lag in treatment from symptom onset (Mean±SD)	3.33±2.01	3.81±2.43	0.41
Duration in days for relief from major symptoms after treatment onset (Mean±SD)	3.52±2.72	3.14±2.14	0.557
Duration in days for relief from minor symptoms after treatment onset (Mean±SD)	4.31±3.91	3.568±2.28	0.57
Need for Escalation of treatment (n)	4	4	0.76
(b) Analysing Mab treatment group participants with treatment onset ≤5 days vs >5 days of symptom onset	**Mab treatment onset ≤5 days, n=49**	**Mab treatment onset >5 days, n=16**	**p-value**
Duration in days for relief from major symptoms after treatment onset (Mean±SD)	3.11±2.39	4.92±3.27	0.019*
Duration in days for relief from minor symptoms after treatment onset (Mean±SD)	3.71±3.24	6.28±5.29	0.023*
Need for Escalation from treatment onset	6	5	0.078

[Table/Fig-5]: Subanalysis for Mab treatment group.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019; *p-value <0.05 was considered statistically significant

Subanalysis for vaccinated and non vaccinated participants amongst the three treatment groups				
Non vaccinated participants	**Remdesivir, n=31**	**Favipiravir, n=13**	**Mab, n=27**	**p-value**
Lag in treatment from symptom onset (Mean±SD)	5.26±2.52	4.39±2.76	3.81±2.43	0.10
Duration in days for relief from major symptoms after treatment onset (Mean±SD)	5.71±2.11	3.62±2.22	3.14±2.14	0.0001
Duration in days for relief from minor symptoms after treatment onset (Mean±SD)	6.38±2.48	5.46±1.85	3.56±2.28	0.00016
Need for escalation from treatment onset (n)	6	3	4	0.44
Parameters for vaccinated participants (two doses):	**Remdesivir, n=13**	**Favipiravir, n=9**	**Mab, n=33**	**p-value**
Lag in treatment from symptom onset (Mean±SD)	5.38±2.21	2.33±2.34	3.33±2.01	0.003
Duration in days for relief from major symptoms after treatment onset (Mean±SD)	4.92±2.14	5±2.55	3.52±2.72	0.139
Duration in days for relief from minor symptoms after treatment onset (Mean±SD)	5.67±2.64	6.89±2.9	4.31±3.92	0.131
Need for escalation from treatment onset (n)	1	4	1	0.0017 (On doing separate analysis for Mab vs Remdesivir p-value=0.49)

[Table/Fig-6]: Subanalysis for vaccinated and non vaccinated participants amongst the three treatment groups.
Mab: Monoclonal antibody; SD: Standard deviation; COVID-19: Coronavirus disease 2019; *p-value <0.05 was considered statistically significant

DISCUSSION

In this present study, a total of 158 participants were included and all had mild to moderate COVID-19 infection. All patients were admitted to the Inpatient Department, despite Casirivimab and imdevimab being authorised for Outpatient Department use due to logistic reasons and as per request of the participants. Participants of Mab group were significantly elder with more co-morbidities, as is the case in other Mab studies too [20]. This is because the drug was initially authorised for adults ≥65 years or with co-morbidities or any other risk for progression to severe disease [21].

Casirivimab and imdevimab are human Immunoglobulin G-1 (IgG1) monoclonal antibodies and are explicitly directed against the spike protein of COVID-19. These prevent the virus from attaching to and entering human cells and thus affecting the progression of disease [22].

In the case of remdesivir, the Ribonucleic Acid (RNA)-dependent RNA polymerase of COVID-19 arrest of RNA synthesis occurs after the incorporation of three additional nucleotides [23]. Remdesivir is classified as a direct-acting antiviral agent that works as a delayed chain terminator [23], arresting viral replication. To the best of authors knowledge there is no study that analyses and compares the three drugs; favipiravir, remdesivir and Mab. Since the ultimate purpose of these drugs is to arrest viral replication, it would be pertinent to compare them.

All participants of this study at the time of treatment onset were haemodynamically stable with no requirement for oxygen or non invasive ventilation (except in cases like Obstructive Sleep Apnea or those who required it even before infection with COVID-19). Mab and favipiravir-treatment group had more mild cases compared to remdesivir-treatment group. As per the Indian Ministry of Health and Family Welfare guidelines [12] guidelines, remdesivir is recommended for patients having some lung involvement or having moderate to severe disease, hence the group had a greater number of patients having moderate COVID-19 infection.

There were two cases of mortality in the Mab treatment group compared to none in the other treatment groups. Of these one of them died due to reasons other than COVID-19 disease. This particular patient had diabetic foot with sepsis along with COVID. The other patient had developed secondary infection during the course of COVID-19 treatment and thus succumbed. As the sample size is limited, it was hence difficult to compare the three groups for risk of mortality.

In the present study for the moderate COVID-19 subgroup, Mab and Remdesivir were comparable for symptom recovery and need for escalation when treatment was initiated within 5 days of symptom onset. Spinner CD et al., [2] randomised patients to a 5-day course of remdesivir, and found a statistically significant difference in clinical status compared with standard care for patients with moderate COVID-19 disease [2]. In a Lancet study, among high-risk patients with mild to moderate COVID-19, Casirivimab–imdevimab treatment was associated with a significantly lower rate of hospitalisation and a thus lower rate of progression of the disease [24].

As per guidelines Mab and remdesivir, both are to be given within 10 days of symptom onset [25,21]. Hence, the present study compared if there was any benefit of starting treatment with Mab within the first five days, vs later. In the present study, Mab treatment group patients whose treatment started on the 5th day or before had earlier symptom recovery compared to Mab treatment group patients who received treatment later. When compared to the remdesivir treatment group, Mab-treatment group fared better than the remdesivir group for the duration/time to symptom recovery, when both had treatment onset within five days of symptoms. Patients with mild COVID-19 disease having received Mab treatment also fared better when compared to mild COVID-19 disease patients who received remdesivir in terms of recovery of symptoms as well as progression of disease. Another study also report that the antibody cocktail of Casirivimab and imdevimab significantly shortened the duration of symptoms by four days (with a median of 10 vs 14 days to clinical improvement (p-value <0.0001). The improvement was best seen among those having baseline negative COVID-19 antibodies [22].

There is very scarce data for comparison of COVID-19 treatment in those patients who have received the COVID-19 vaccination vs the non vaccinated patients. Non vaccinated patients receiving Mab or favipiravir treatment recovered earlier than the remdesivir group but the need for escalation was comparable in all three treatment groups. In the vaccinated subgroup, all three treatment groups had comparable symptom recovery, this could be because vaccination itself is said to reduce the disease severity [24]. No difference was found in vaccinated and non vaccinated patients of the Mab group when compared for the need of treatment escalation and symptom recovery. No participant of this study had any adverse event related to any of the drugs used.

To the best of authors knowledge, this is the first study that compares Mab therapy with other treatment modalities. All the other previous studies compare each modality with a placebo therapy. Also, authors believe that the present study is the first study to include the subanalysis of COVID-19 vaccinated versus non vaccinated participants and compare the treatment response with various treatment modalities available.

Limitation(s)

The sample size was small and it was a retrospective study. The Mab treatment group had more elderly patients with co-morbidities.

These could be confounding factors when analysing the response to treatment and progression of disease of COVID-19 patients. Larger sample size and randomisation of patients would make further subanalysis possible with age and individual co-morbidities and this would help to fully understand the benefit of this cocktail drug. As genomic sequencing was not possible, different variants of COVID-19 virus were not assessed.

CONCLUSION(S)

As per the study findings, the recovery from symptoms was earlier when treated with Mab treatment therapy for patients with mild COVID-19 disease or when treatment onset was ≤5 days from symptom onset. Although the numbers were small no patient in the Mab treatment group required escalation of treatment in the mild group compared to the other treatment groups. Secondly, patients in the moderate COVID-19 disease subgroup receiving Mab vs remdesivir treatment had comparable recovery time and disease progression. Non vaccinated patients receiving Mab therapy recovered from minor symptoms earlier than the remdesivir treatment group. No difference was found in COVID-19 vaccinated and unvaccinated patients of the Mab-treatment group when compared for the need of treatment escalation and symptom recovery. Hence, authors recommend use of monoclonal antibody therapy for all patients with mild disease and when symptom duration is five days or less.

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