Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

American Journal of Emergency Medicine 50 (2021) 129–131

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Real world utilization of REGEN-COV2 at a community hospital

Jordan Ash, BS, BA [a], Rachael Leavitt, BS, MS [b], Tyson Dietrich, PharmD [c], Sarah Schritter, RN [d], James Wells, RN [d], Anthony Santarelli, PhD [e], John Ashurst, DO, MSc [f,*]

[a] Arizona College of Osteopathic Medicine, USA
[b] Rocky Vista University College of Osteopathic Medicine, USA
[c] Department of Pharmacy, Kingman Regional Medical Center, USA
[d] Department of Nursing, Kingman Regional Medical Center, USA
[e] Department of Graduate Medical Education, Kingman Regional Medical Center, USA
[f] Department of Emergency Medicine, Kingman Regional Medical Center, USA

ARTICLE INFO

Article history:
Received 5 February 2021
Received in revised form 16 July 2021
Accepted 19 July 2021

Keywords:
COVID-19
Monoclonal antibody
REGN-COV2
Casirivimab
Imdevimab

ABSTRACT

Introduction: Monoclonal antibodies received an Emergency Use Authorization (EUA) from the U.S. Food & Drug Administration for the outpatient treatment of mild to moderate coronavirus disease 2019 (COVID-19). REGN-COV2, casirivimab and imdevimab, has been shown to decrease the viral load and healthcare visits of those with mild to moderate COVID-19 who are treated in the outpatient setting.
Objective: To determine 7- and 14-day emergency department (ED) and hospitalization rates of adult patients given REGN-COV2 for the outpatient treatment of COVID-19 at a community hospital.
Methods: A convenience sample of consecutive adult patients given REGN-COV2 from January 18, 2021 through March 31, 2021 for the outpatient treatment of mild to moderate COVID-19. Abstracted data included patient demographics, allergic reactions, ED presentations and hospitalizations at 7 and 14 days, and in-hospital mortality.
Results: A total of 68 patients with a medain age of 69 years (IQR 57–75.5) and 58.3% being female were given REGEN-COV2 during the study period. No allergic reactions were noted during infusion. Of those infused, 18% (12/68) were infused in the ED and had a median length of stay of 477 min. Following infusion, 10% (7/68) of patients re-presented to the ED and 2% (1/68) were hospitalized for COVID-19 at 14 days. In those aged 65 years or greater, 12% (5/42) of patients re-presented to the ED following infusion. Of those who re-presented to the emergency department, the median age was 72.5 years and the median time from infusion to re-presentation was 2.0 days. No patients suffered in-hospital mortality during the study period.
Conclusion: There was a significant length of stay associated with REGN-COV2 infusion in the emergency department. Following REGN-COV2 infusion, few patients under the age of 65 re-presented to the emergency department at seven and 14 days. However, a large number of patients aged over 65 years re-presented to the ED following infusion.

1. Introduction

Since the emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), physicians and scientists have searched for an outpatient treatment option for those with coronavirus disease 2019 (COVID-19). REGN-COV2 (casirivimab and imdevimab), a cocktail composed of two non-competing, neutralizing human IgG1 antibodies that targets the spike protein of SARS-CoV-2, was recently given emergency use authorization (EUA) by the U.S. Food and Drug Administration for the outpatient treatment of mild to moderate COVID-19 [1,2]. In an animal model, REGN-COV2 was shown to reduce viral loads of SARS-CoV-2 and improved viral clearance when given therapeutically [3]. In human trials, data showed a decrease in respiratory viral load and healthcare visits in those who received REGN-COV2 as compared to a placebo [1]. Recently a phase 3 trial showed a 71.3% reduction in hospitalizations and a 70.4% reduction in all-cause mortality in those who received REGN-COV2 as compared to a placebo [4]. However, little clinical data is currently available on the real-world utilization and outcomes of those who have received REGN-COV2 in the community setting. The primary objective the study was to determine 7- and 14-day emergency department (ED) and hospitalization rates of adult

* Corresponding author.
E-mail addresses: TDietrich@azkrmc.com (T. Dietrich), SSchritter@azkrmc.com (S. Schritter), James.Wells@azkrmc.com (J. Wells), Anthony.Santarelli@azkrmc.com (A. Santarelli), Ashurst.john.32.research@gmail.com (J. Ashurst).

https://doi.org/10.1016/j.ajem.2021.07.050
0735-6757/

patients given REGN-COV2 for the outpatient treatment of COVID-19 at a community hospital.

2. Methods

2.1. Setting

Kingman Regional Medical Center (KRMC) is a 235-bed community hospital located in northern Arizona with an annual ED volume of approximately 50,000 patient visits per year. During the study period there was a 9% decrease in ED visits from the previous year. A total of 655 cases of COVID-19 were diagnosed by the hospital from January 18, 2021 through March 31, 2021.

2.2. Study protocol

Following institutional review board approval, a convenience sample of consecutive adults aged 18 years old or older who received the outpatient administration of REGN-COV2 from January 18, 2021 through March 31, 2021 were included in analysis. Physicians screened patients on a daily basis who had positive results from a direct SARS-CoV-2 viral test for those who met one of the criteria for administration of REGN-COV2 specified by the EUA. A physician then spoke with each patient to discuss the risks and benefits of REGN-COV2 infusion. Following patient agreement, REGN-COV2 was administered by qualified nursing staff at either an outpatient infusion center or the ED. Each patient received a combination dose of 1200 mg of casirivimab and 1200 mg of imdevimab as a single intravenous infusion over 60 min via an infusion pump within 10 days of symptom onset. Patients were monitored for one hour following infusion to assess for any adverse infusion reactions.

All data reported were abstracted from patient charts from the MEDITECH EXPANSE Platform (Medical Information Technology INC, Westwood, MA). Abstracted data included: Patient age, ethnicity, gender, body mass index, smoking status, and authorized use qualifiers. Patients were then tracked daily for return visits to the KRMC ED and admissions to the KRMC in-patient COVID-19 Unit. Patients were not tracked for hospital admissions or ED visits occurring at other sites. All data was abstracted by two trained research assistants who were blinded to the study's primary objective. Research assistants were trained on proper data abstraction prior to the collection of data by the study team. This was completed by a member of the study team abstracting data with the research assistants. With adherence to a quality-controlled protocol and structured abstraction tool, research assistants manually collected all data points. Abstractor monitoring and verification of the independent variables was completed by the primary investigator. Cases for which the two abstractors disagreed on the primary inclusion variables were assessed by the primary investigator for inclusion. Patients with incomplete data following abstraction were removed from analysis.

2.3. Statistical analysis

Data were analyzed using SPSS statistics (IBM Corp., Armonk, New York). Patient demographics and outcomes are reported with descriptive statistics.

3. Results

Of the 655 cases of COVID-19 diagnosed during the study period, a total of 68 patients were given REGN-COV2 with 12 patients (18%) being infused while in the ED. Of those infused in the ED, the median age was 69 years (IQR 57–75.5), 58% were female, and the median length of stay was 447 (IQR 372–522) minutes. No patients had an allergic reaction either during infusion or in the immediate post-infusion period. The median age of those who received REGN-COV2 was 69.0 (IQR 58–76) years with 54% (37/68) being female and a median body mass index of 31.1 (IQR 26.8–35.5). A total of 62% (42/68) of all patients infused were aged 65 or older. Across the cohort a large proportion of patients had a history of hypertension (60%), diabetes (32%) or chronic kidney disease (12%) (Table 1). The median number of risk factors for those infused with REGEN-COV2 was two.

In the total cohort, 10% (7/68) of patients sought further care in the ED with 2% (1/68) of all patients being hospitalized due to a COVID-19 complication within seven days of REGN-COV2 infusion (Table 2). No patients presented to the ED between days eight and 14 following REGN-COV2 infusion. Of those who re-presented to the ED, the median age was 72.5 (IQR 64–81) years with 86% (6/7) being female. The average length of time from infusion to representation to the ED was 2 (IQR 0.5–3.5) days. The one patient hospitalized due to hypoxia was 10 days into her illness and one day following REGN-COV2 infusion. Upon re-presentation to the ED, she required 4 l of oxygen at rest and 6 l with ambulation. She had an inpatient length of stay of six days and was discharged following treatment with remdesivir, dexamethasone, and convalescent plasma. The patient was discharged to home with requiring 2 l of nasal cannula due to hypoxia with ambulation. In those aged 65 years or greater, 12% (5/42) of patients re-presented to the ED following infusion with 0% being hospitalized at seven and 14 days due to a COVID-19 complication. No patients suffered from in-hospital mortality during the study period.

4. Discussion

Data has shown that ED overcrowding and an increased length of stay has a negative impact on patient outcomes [5,6]. Based upon the current data, those infused in the ED had a significant length of stay during the second wave of the COVID-19 pandemic. This increased length of stay may have resulted in an increased length of stay for other patients causing a possible increase in negative outcomes. The feasibility of infusion within the ED could be limited due to patient volumes, lack of available patient care space, the length of time to perform tests, the time needed for each infusion, and the FDA required monitoring period post infusion [7]. Healthcare organizations should look to alternative locations, including outpatient infusion centers, for monoclonal antibody infusion to alleviate the burden on EDs.

The current data showed that an older patient population was more likely to receive REGN-COV2 compared to the original research on the medication and the recent publication of the phase 3 trial [1,4]. The study also showed that those to receive REGN-COV2 during the study period had a higher prevalence of risk factors for progression of disease as compared to previous literature [1,4]. It is unclear for the difference in patient ages and increased prevalence of risk factors between the current study and previously reported literature but could be due to the geographic location of the institution and the population being served.

Both the overall cohort and the elderly population was also more likely to present to the ED for further care due to COVID-19 following

Table 1
Emergency use authorization patient qualifiers for those infused with REGN-COV2.

Authorized use qualifier	Patients
Body mass index (BMI) ≥35	18 (27%)
Chronic kidney disease	8 (12%)
Diabetes	22 (32%)
Immunosuppressive disease	4 (6%)
Currently receiving immunosuppressive treatment	3 (4%)
Hypertension	41 (60%)
Congestive heart failure	2 (3%)
Chronic obstructive pulmonary disease	10 (15%)
Are ≥65 years of age	42 (62%)
Are ≥55 years of age and have cardiovascular disease or hypertension or chronic obstructive pulmonary disease/other chronic respiratory disease	26 (38%)

Table 2
Hospitalizations and Emergency Department Visits among Patients who received REGN-COV2.

	Hospitalized		Emergency Care	
	7(d)	14(d)	7(d)	14(d)
Total Cohort ($N = 68$)	1 (2%)	1 (2%)	7 (10%)	7 (10%)
Aged Over 65 ($N = 42$)	0 (0%)	0 (0%)	5 (12%)	5 (12%)

infusion than previously reported [1,4]. This difference is most likely related to the number of risk factors seen in the current population and the time to presentation prior to infusion with REGN-COV2. Current data has shown that those with increased risk factors such as age, hypertension or diabetes are at an increased risk for progression of COVID-19 that may require hospitalization [7,8,9]. Despite the patient demographics in the current study, no patients in the 65 year or older age group were hospitalized due to a COVID-19 complication at 14 days following infusion.

5. Limitations

The location and population characteristics of those treated at Kingman Regional Medical Center may not allow these results to be generalizable across all patient populations in rural communities. Patients were offered treatment based upon medication availability (bamlanivimab versus REGN-COV2), symptom onset, physician preference, and risk factors for progression of disease per the EUA. However, it is unclear the number of patients who were offered monoclonal antibody treatment and declined therapy. Patients were referred to the outpatient infusion center when able for infusion from the ED due to increased volumes of respiratory and critical care patients seen with the second wave of the pandemic. This may have decreased the number of patients treated within the ED. County coroner records were not reviewed to confirm mortality in patients who received REGN-COV2.

6. Conclusion

A significant length of stay was associated with infusion of REGN-COV2 within the ED. Few patients under the age of 65 re-presented to the ED following infusion but a larger proportion of the elderly did present to the ED following infusion. In order to improve departmental flow, programs should be targeted at early diagnosis, identification, and location of medication administration to alleviate both ED and potentially in-patient burdens due to COVID-19. However, further large-scale randomized control trials are needed to assess the true treatment effect of REGEN-COV2 in a community setting prior to it being considered the standard of care for those with mild to moderate COVID-19 in the outpatient setting.

Author contributions

All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors drafted the article or revised it critically for important intellectual content; authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Competing Interest

All authors have no conflicts of interest to disclose associated with this project.

References

[1] Weinreich DM, Sivapalasingman S, Norton T, et al. REGN-COV2, a neutralizing antibody cocktail, in outpatients with COVID-19. N Engl J Med. 2021;384(3):238–51.
[2] FDA News Release. Coronavirus (COVID-19) update: FDA authorizes monoclonal antibody for treatment of COVID-19 Published November 21, 2020. Accessed February 3 2021; https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibodies-treatment-covid-19.
[3] Baum A, Ajithdoss D, Copin R, et al. REGN-COV2 antibodies prevent and treat SARS-CoV-2 infection in rhesus macaques and hamsters. Science. 2020;370:1110–5.
[4] Weinrech D, Sivapaasaingman S, Norton T, et al. REGEN-COV antibody cocktail clinical outcomes study in COVID-19 outpatients. medRxIV. 2021;342:d2983 [Pre-Print].
[5] Guttman A, Schull MJ, Vermeulen MJ, Stukel TA. Association between waiting and short term mortality and hospital admission after departure from emergency department: population based cohort study from Ontario. Canada BMJ. 2011;342:d2983.
[6] McCusker J, Vadeboncoeur A, Levesque JF, et al. Increase in emergency department occupancy are associated with adverse 30-day outcomes. Acad Emerg Med. 2014;21(10):1092–100.
[7] Fact Sheet for Healthcare Providers Emergency Use Authorization (EUA) of Casirivimab and Imdevimab. Published November 21; 2020 Accessed February 12 https://www.fda.gov/media/143892/download.
[8] Pijls BG, Jolani S, Atherley A, et al. Demographic risk factors for COVID-19 infection severity, ICU admission, and death: a meta-analysis of 59 studies. BMJ. 2021;11(1):e044640.
[9] Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: a systematic review and meta-analysis. J Infect. 2020;81(2):e16–25.