SPPH Journal of Rare Diseases and Orphan Drugs, V1, 2020

Original research

OUTCOME OF COVID-19 AND MATCH-POPULATION ANALYSIS WITH COMPASSIONATE USE OF REMDESIVIR

Olga Vasylyeva[1*], Tara Chen[1], John Hanna[1]

Author information: *1[1]Infection Disease Department, Rochester General Hospital; 1425 Portland Ave, Rochester, NY 14621; email: olga.vasylyeva@rochesterregional.org*

Abstract: ***Objectives:*** To analyze treatment outcomes for patients with COVID-19 with and without compassionate use of Remdesivir.

Methods: A retrospective review of electronic medical records for patients who did not receive Remdesivir due to unavailability. Match-population analysis based on inclusion criteria for compassionate use Remdesivir of the patient population who received Remdesivir as reported in literature and patients without Remdesivir.

Results: Sixty-six percent of patients met the criteria for compassionate use Remdesivir, 41% required intensive care unit admission, 20% invasive ventilation, and 10% died. The median time of hospitalization for survivors was eight days.

In the separate group of patients who did not meet the criteria for compassion use Remdesivir, mortality among patients with CrCl > 30 ml min, an exclusion criterion, was significantly higher as compared with patients with CrCl < 30 ml min.

Conclusion: When compared with previously reported data from patients who received compassionate use Remdesivir, our population had notably fewer patients requiring invasive ventilation.

Keywords: COVID-19, SARS-CoV-2, Remdesivir

INTRODUCTION COVID-19 is a disease caused by the SARS-CoV-2 that can result in the severe systemic inflammatory response and respiratory failure. As of July 2020, 140,828 people died due to COVID-19 in the United States [1,2].

Remdesivir has demonstrated activity against MERS, SARS, and SARS-CoV-2 *in vitro* [3]. In January 2020, Gilead Sciences began accepting requests for compassionate use of Remdesivir, however on March 22, 2020, Gilead Sciences introduced limitations on compassionate use due to overwhelming demand [4,5]. Rochester Regional Health (RRH) has hospitalized a number of COVID-19 patients who did not receive Remdesivir due to its unavailability.

On April 10, 2020, multicenter data were published by Grein J. et al. on compassionate use of Remdesivir for patients with severe COVID-19 based on the FDA and Gilead Sciences approval before the restriction, but the study lacked a control group [5].

The aim of this study was to analyze treatment outcomes of the COVID-19 patients admitted to RRH and compare their outcomes to a subgroup matched to Grein's study population who received compassionate care Remdesivir.

METHODS A retrospective review of the patients' electronic medical records who were hospitalized due to COVID-19 between March 22, 2020, and April 30, 2020, was performed following RRH IRB approval.

A subgroup of patients was selected to match the inclusion criteria to those who received compassionate care Remdesivir as reported by Grein J. et al. and Gilead Sciences. The inclusion criteria were: hospitalized patients with laboratory-confirmed SARS-CoV-2 by polymerase chain reaction; oxygen saturation of 94% or less while the patient was breathing ambient air or a need for oxygen support; creatinine clearance (CrCl) > 30 ml per minute

*Corresponding author: Olga Vasylyeva, Infection Disease Department, Rochester General Hospital; 1425 Portland Ave, Rochester, NY 14621; email: olga.vasylyeva@rochesterregional.org

upon admission; and aspartate aminotransferase (AST) and alanine aminotransferase (ALT) less than five times the upper limit of normal range upon admission.

We also analyzed outcomes for the patients in our population who did not meet inclusion criteria to receive compassionate care Remdesivir.

The primary outcomes were a need for invasive ventilation and mortality.

RESULTS During the studied period, 149 patients with laboratory-confirmed COVID-19 were hospitalized at RRH. Among these patients, 98 (66%) met inclusion criteria for the compassionate use of Remdesivir.

The median age in our subgroup was 64 (27-97) years, and 62 (63%) were male. Forty (41%) patients required intensive care unit admission, and 20 (20%) required invasive ventilation. Ten patients died (10%) with a median time from admission to death of 9 days. The median time of hospitalization for survivors was 8 days (Table 1).

DISCUSSION In our population of patients who met the criteria for compassionate care Remdesivir, but did not receive it because of unavailability, 10 (10%) patients died.

When compared with the population presented by Grein J. et al., we observed that fewer people required invasive ventilation (20% vs. 64%) in our population, which could reflect variability in disease severity between groups, and influence mortality (10% vs. 13%).

Furthermore, patients in our population who presented with CrCl< 30 per min and therefore were not qualified for Remdesivir treatment, had significantly higher mortality as compared with patients who met the criteria to receive Remdesivir (36% vs. 10%).

The limitations of this study were the absence of randomization and lack of sufficient matching to perform statistical analysis of differences because we did not have raw data from the group that received Remdesivir.
On May 22, 2020, a preliminary report from a clinical trial

Baseline Characteristics and Outcomes	Received compassionate care Remdesivir (Grein J. et al.)	No Remdesivir (RRH), but meeting inclusion criteria	No Remdesivir (RRH), not meeting inclusion criteria
Total number of patients	53	98	51
Median age, yr	64	64	67
Male sex, n (%)	40 (75%)	62 (63%)	28 (54%)
Duration of hospitalization (survivors), median	Unknown	8 days (from 1 to 42 days)	3 days (from 1 to 48 days)
Invasive ventilation, n (%)	34 (64%)	20 (20%)	10 (20%)
Death, n (%)	7 (13%)	10 (10%)	8 (16%)

Table 1. Baseline characteristics and outcomes

In the group of RRH patients that were not qualified to receive Remdesivir based on inclusion criteria (51 patients), the mortality was 16%. Twenty-two patients were not qualified due to CrCl< 30 ml per min upon admission. Eight of the patients with low CrCl (36%) required invasive ventilation, and eight of the 22 patients died, which was significantly more than patients with CrCl> 30 ml min (36% vs. 10%, $p < .05$ by Chi-square).

that compared Remdesivir and placebo for treatment of COVID-19 was published [6,7]. Preliminary results showed 10.7% mortality in the placebo group, which is comparable with the 10% in our population, and 5.9% in the Remdesivir group. In this clinical trial, the difference in mortality between placebo and intervention groups was not statistically significant. The median time to recovery, defined in this trial as either discharge or continuous

hospitalization for infection-control purposes, significantly decreased from 15 to 11 days. However, in our population the median time of hospitalization was 8 days, therefore it is uncertain if we would observe this benefit in our population.

In conclusion, in our population mortality among people who met inclusion criteria for compassionate use of Remdesivir but did not receive the drug due to unavailability was 10% with the median time to recovery for survivors of 8 days. There was significantly higher mortality among patients who presented with CrCl < 30 ml per min, an exclusion criterion for compassionate use of Remdesivir. The benefit of Remdesivir in this population needs further evaluation.

CONCLUSION When compared with previously reported data from patients who received compassionate use Remdesivir, our population had notably fewer patients requiring invasive ventilation.

REFERENCES

1. World Health Organization (WHO). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) [Internet]. [cited 2020 Jun 12]. Available: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf?fbclid=IwAR1k-CfPkkBnSshMxATg_HA6Bm5Y-nIoLKAXEl2SmTklooTJY42IcQ1oI00.
2. Johns Hopkins University of Medicine Coronavirus Resource Center. COVID-19 Map [Internet]. [cited 2020 Jul]. Available: https://coronavirus.jhu.edu/map.html?fbclid=IwAR0WthjsAIT3BkIApe7gjVazepLLf8rYMJohq7zEY2NgetQa2wEwss4DNlA.
3. Li G, Clercq ED. Therapeutic options for the 2019 novel coronavirus (2019-nCoV). Nat Rev. 2020;19:149-50. Available: https://media.nature.com/original/magazine-assets/d41573-020-00016-0/d41573-020-00016-0.pdf.
4. Gilead Sciences. Gilead Sciences Statement on Access to Remdesivir Outside of Clinical Trials. 2020 Mar 22 [Internet]. [cited 2020 Jul]. Available: https://www.gilead.com/news-and-press/company-statements/gilead-sciences-statement-on-access-to-remdesivir-outside-of-clinical-trials.
5. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. N Engl J Med 2020;382:2327-2336. DOI: 10.1056/NEJMoa2007016.
6. National Institute of Allergy and Infectious Diseases (NIAID). Adaptive COVID-19 Treatment Trial. NIH. US National Library of Medicine ClinicalTrials.gov [Internet]. [cited 2020 Jul]. Available: https://clinicaltrials.gov/ct2/show/NCT04280705.
7. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for treatment of Covid-19–preliminary report. N Engl J Med. 2020 May 22. DOI: 10.1056/NEJMoa2007764.