



ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

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Abstract

BACKGROUND

Remdesivir, a nucleotide analogue prodrug that inhibits viral RNA polymerases, has shown in vitro activity against SARS-CoV-2.

METHODS

We provided remdesivir on a compassionate-use basis to patients hospitalized with Covid-19, the illness caused by infection with SARS-CoV-2. Patients were those with confirmed SARS-CoV-2 infection who had an oxygen saturation of 94% or less while they were breathing ambient air or who were receiving oxygen support. Patients received a 10-day course of remdesivir, consisting of 200 mg administered intravenously on day 1, followed by 100 mg daily for the remaining 9 days of treatment. This report is based on data from patients who received remdesivir during the period from January 25, 2020, through March 7, 2020, and have clinical data for at least 1 subsequent day.

RESULTS

Of the 61 patients who received at least one dose of remdesivir, data from 8 could not be analyzed (including 7 patients with no post-treatment data and 1 with a dosing error). Of the 53 patients whose data were analyzed, 22 were in the United States, 22 in Europe or Canada, and 9 in Japan. At baseline, 30 patients (57%) were receiving mechanical ventilation and 4 (8%) were receiving extracorporeal membrane oxygenation. During a median follow-up of 18 days, 36 patients (68%) had an improvement in oxygen-support class, including 17 of 30 patients (57%) receiving mechanical ventilation who were extubated. A total of 25 patients (47%) were discharged, and 7 patients (13%) died; mortality was 18% (6 of 34) among patients receiving invasive ventilation and 5% (1 of 19) among those not receiving invasive ventilation.

CONCLUSIONS

In this cohort of patients hospitalized for severe Covid-19 who were treated with compassionate-use remdesivir, clinical improvement was observed in 36 of 53 patients (68%). Measurement of efficacy will require ongoing randomized, placebo-controlled trials of remdesivir therapy. (Funded by Gilead Sciences.)

Introduction



SINCE THE FIRST CASES WERE REPORTED IN DECEMBER 2019, INFECTION with the severe acute respiratory coronavirus 2 (SARS-CoV-2) has become a worldwide pandemic.^{1,2} Covid-19 — the illness caused by SARS-CoV-2 — is overwhelming health care systems globally.^{3,4} The symptoms of SARS-CoV-2 infection vary widely, from

asymptomatic disease to pneumonia and life-threatening complications, including acute respiratory distress syndrome, multisystem organ failure, and ultimately, death.⁵⁻⁷ Older patients and those with preexisting respiratory or cardiovascular conditions appear to be at the greatest risk for severe complications.^{6,7} In the absence of a proven effective therapy, current management consists of supportive care, including invasive and noninvasive oxygen support and treatment with antibiotics.^{8,9} In addition, many patients have received off-label or compassionate-use therapies, including antiretrovirals, antiparasitic agents, antiinflammatory compounds, and convalescent plasma.¹⁰⁻¹³

Remdesivir is a prodrug of a nucleotide analogue that is intracellularly metabolized to an analogue of adenosine triphosphate that inhibits viral RNA polymerases. Remdesivir has broad-spectrum activity against members of several virus families, including filoviruses (e.g., Ebola) and coronaviruses (e.g., SARS-CoV and Middle East respiratory syndrome coronavirus [MERS-CoV]) and has shown prophylactic and therapeutic efficacy in nonclinical models of these coronaviruses.¹⁴⁻¹⁷ In vitro testing has also shown that remdesivir has activity against SARS-CoV-2. Remdesivir appears to have a favorable clinical safety profile, as reported on the basis of experience in approximately 500 persons, including healthy volunteers and patients treated for acute Ebola virus infection,^{18,19} and supported by our data (on file and shared with the World Health Organization [WHO]). In this report, we describe outcomes in a cohort of patients hospitalized for severe Covid-19 who were treated with remdesivir on a compassionate-use basis.

Methods



PATIENTS

Gilead Sciences began accepting requests from clinicians for compassionate use of remdesivir on January 25, 2020. To submit a request, clinicians completed an assessment form with demographic and disease-status information about their patient (see the [Supplementary Appendix](#), available with the full text of this article at NEJM.org). Approval of requests was reserved for hospitalized patients who had SARS-CoV-2 infection confirmed by reverse-transcriptase–polymerase-chain-reaction assay and either an oxygen saturation of 94% or less while the patient was breathing ambient air or a need for oxygen support. In addition, patients were required to have a creatinine clearance above 30 ml per minute and serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) less than five times the upper limit of the normal range, and they had to agree not to use other investigational agents

for Covid-19.

In approved cases, the planned treatment was a 10-day course of remdesivir, consisting of a loading dose of 200 mg intravenously on day 1, plus 100 mg daily for the following 9 days. Supportive therapy was to be provided at the discretion of the clinicians. Follow-up was to continue through at least 28 days after the beginning of treatment with remdesivir or until discharge or death. Data that were collected through March 30, 2020, are reported here. This open-label program did not have a predetermined number of patients, number of sites, or duration. Data for some patients included in this analysis have been reported previously.²⁰⁻²² Details of the study design and conduct can be seen in the [protocol](#) (available at NEJM.org).

STUDY ASSESSMENTS

Data on patients' oxygen-support requirements, adverse events, and laboratory values, including serum creatinine, ALT, and AST, were to be reported daily, from day 1 through day 10, and additional follow-up information was solicited through day 28. Although there were no prespecified end points for this program, we quantified the incidence of key clinical events, including changes in oxygen-support requirements (ambient air, low-flow oxygen, nasal high-flow oxygen, noninvasive positive pressure ventilation [NIPPV], invasive mechanical ventilation, and extracorporeal membrane oxygenation [ECMO]), hospital discharge, and reported adverse events, including those leading to discontinuation of treatment, serious adverse events, and death. In addition, we evaluated the proportion of patients with clinical improvement, as defined by live discharge from the hospital, a decrease of at least 2 points from baseline on a modified ordinal scale (as recommended by the WHO R&D Blueprint Group), or both. The six-point scale consists of the following categories: 1, not hospitalized; 2, hospitalized, not requiring supplemental oxygen; 3, hospitalized, requiring supplemental oxygen; 4, hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both; 5, hospitalized, requiring invasive mechanical ventilation, ECMO, or both; and 6, death.

PROGRAM OVERSIGHT

Regulatory and institutional review board or independent ethics committee approval was obtained for each patient treated with remdesivir, and consent was obtained for all patients in accordance with local regulations. The program was designed and conducted by the sponsor (Gilead Sciences), in accordance with the [protocol](#). The sponsor collected the data, monitored conduct of the program, and performed the statistical analyses. All authors had access to the data and assume responsibility for the integrity and completeness of the reported data. The initial draft of the manuscript was prepared by a writer employed by Gilead Sciences along with one of the authors, with input from all the authors.

STATISTICAL METHODS

No sample-size calculations were performed. The analysis population included all patients who received their first dose of remdesivir on or before March 7, 2020, and for whom clinical data for at least 1 subsequent day were available. Clinical improvement and mortality in the remdesivir compassionate-use cohort were described with the use of Kaplan–Meier analysis. Associations between pretreatment characteristics and these outcomes were evaluated with Cox proportional hazards regression. Because the analysis did not include a provision for correcting for multiple comparisons in tests for association between baseline variables and outcomes, results are reported as point estimates and 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiple comparisons, so the intervals should not be used to infer definitive associations with outcomes. All analyses were conducted with SAS software, version 9.4 (SAS Institute).

Results

PATIENT RANDOMIZATION

In total, 61 patients received at least one dose of remdesivir on or before March 7, 2020; 8 of these patients were excluded because of missing postbaseline information (7 patients) and an erroneous remdesivir start date (1 patient) (Fig. S1 in the [Supplementary Appendix](#)). Of the 53 remaining patients included in this analysis, 40 (75%) received the full 10-day course of remdesivir, 10 (19%) received 5 to 9 days of treatment, and 3 (6%) fewer than 5 days of treatment.

BASELINE CHARACTERISTICS OF THE PATIENTS

Table 1.

Table 1. Baseline Demographic and Clinical Characteristics of the Patients.*

Characteristic	Invasive Ventilation (N=34)	Noninvasive Oxygen Support (N=19)	Total (N=53)
Median age (IQR) — yr	67 (56–72)	53 (41–68)	64 (48–71)
Age category — no. (%)			
<50 yr	6 (18)	8 (42)	14 (26)
50 to <70 yr	14 (41)	7 (37)	21 (40)
≥70 yr	14 (41)	4 (21)	18 (34)
Male sex — no. (%)	27 (79)	13 (68)	40 (75)
Region — no. (%)			
United States	14 (41)	8 (42)	22 (42)
Japan	8 (24)	1 (5)	9 (17)
Europe or Canada	12 (35)	10 (53)	22 (42)
Oxygen-support category — no. (%)			
Invasive ventilation	34 (100)	—	34 (64)
Invasive mechanical ventilation	30 (88)	—	30 (57)
Extracorporeal membrane oxygenation	4 (12)	—	4 (8)
Noninvasive oxygen support	—	19 (100)	19 (36)
Noninvasive positive-pressure ventilation	—	2 (11)	2 (4)
High-flow oxygen	—	5 (26)	5 (9)
Low-flow oxygen	—	10 (53)	10 (19)
Ambient air	—	2 (11)	2 (4)
Median duration of symptoms before remdesivir therapy (IQR) — days	11 (8–15)	13 (10–14)	12 (9–15)
Coexisting conditions — no. (%)			
Any condition	25 (74)	11 (58)	36 (68)
Hypertension	9 (26)	4 (21)	13 (25)
Diabetes	8 (24)	1 (5)	9 (17)
Hyperlipidemia	6 (18)	0	6 (11)
Asthma	5 (15)	1 (5)	6 (11)
Median laboratory values (IQR)			
ALT — IU per liter	48 (31–79)	27 (20–45)	37 (25–61)
AST — IU per liter	39 (30–76)	35 (28–46)	36 (29–67)
Creatinine — mg per deciliter	0.90 (0.66–1.17)	0.79 (0.63–1.00)	0.89 (0.64–1.08)

* ALT denotes alanine aminotransferase, AST aspartate aminotransferase, and IQR interquartile range. To convert the values for creatinine to micromoles per liter, multiply by 88.4.

Baseline Demographic and Clinical Characteristics of the Patients.

Table 1 shows baseline demographic and clinical characteristics of the 53 patients in the compassionate-use cohort. Patients were enrolled in the United States (22 patients), Japan (9), Italy (12), Austria (1), France (4), Germany (2), Netherlands (1), Spain (1), and Canada (1). A total of 40 patients (75%) were men, the age range was 23 to 82 years, and the median age was 64 years (interquartile range, 48 to 71). At baseline, the majority of patients (34 [64%]) were receiving invasive ventilation, including 30 (57%) receiving mechanical ventilation and 4 (8%) receiving ECMO. The median duration of invasive mechanical ventilation before the initiation of remdesivir treatment was 2 days (interquartile range, 1 to 8). As compared with patients who were receiving noninvasive oxygen support at baseline, those receiving invasive ventilation tended to be older (median age, 67 years, vs. 53 years), were more likely to be male (79%, vs. 68%), had higher median serum ALT (48 U per liter, vs. 27) and creatinine (0.90 mg per deciliter, vs. 0.79 [79.6 μ mol per liter, vs. 69.8]), and a higher prevalence of coexisting conditions, including hypertension (26%, vs. 21%), diabetes (24%, vs. 5%), hyperlipidemia (18%, vs. 0%), and asthma (15%, vs. 5%). The median duration of symptoms before the initiation of remdesivir treatment was 12 days (interquartile range, 9 to 15) and did not differ

substantially between patients receiving invasive ventilation and those receiving noninvasive ventilation (Table 1).

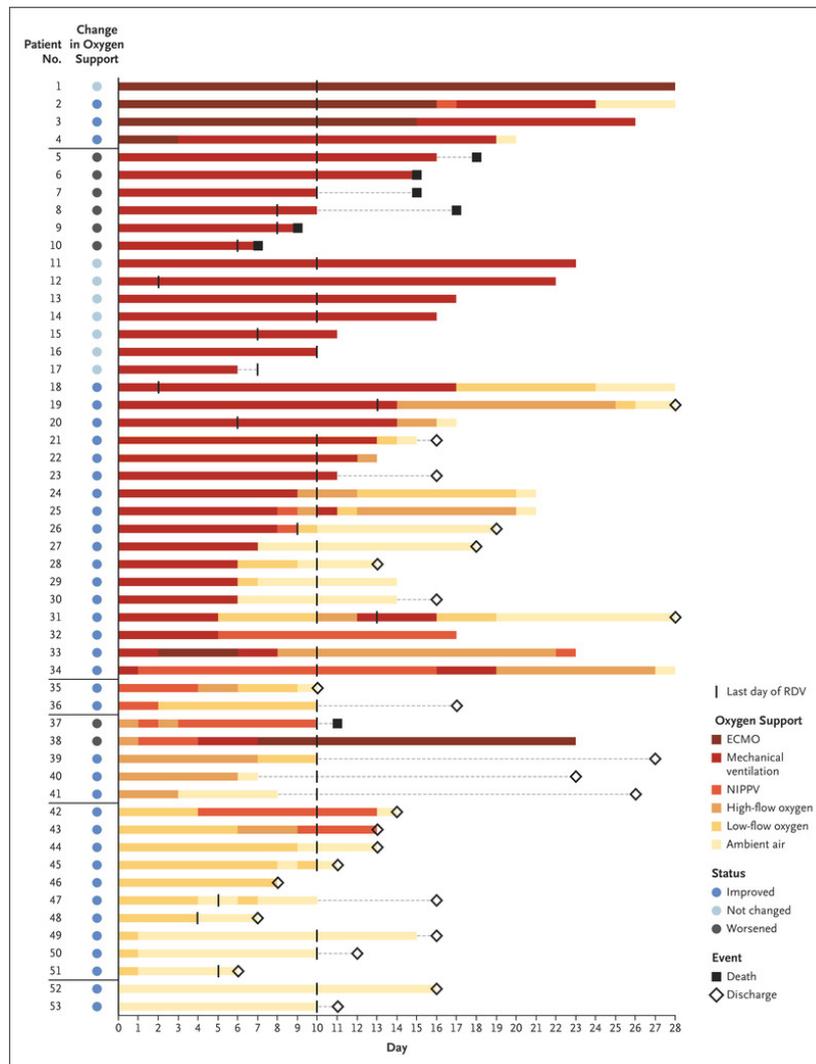
CLINICAL IMPROVEMENT DURING REMDESIVIR TREATMENT

Figure 1.

		No. of Patients in Oxygen-Support Group at Baseline (%)			
		Invasive (N=34)	Noninvasive (N=7)	Low-flow oxygen (N=10)	Ambient air (N=2)
No. of Patients in Oxygen-Support Group after Treatment (%)	Category on ordinal scale →	5	4	3	2
	Death	6 (18)	1 (14)	0	0
	Invasive	9 (26)	1 (14)	0	0
	Noninvasive	3 (9)	0	0	0
	Low-flow oxygen	0	0	0	0
	Ambient air	8 (24)	0	0	0
	Discharged	8 (24)	5 (71)	10 (100)	2 (100)
	Improvement	19 (56)	5 (71)	10 (100)	2 (100)
	↑				
	Category on ordinal scale				

Oxygen-Support Status at Baseline and after Treatment.

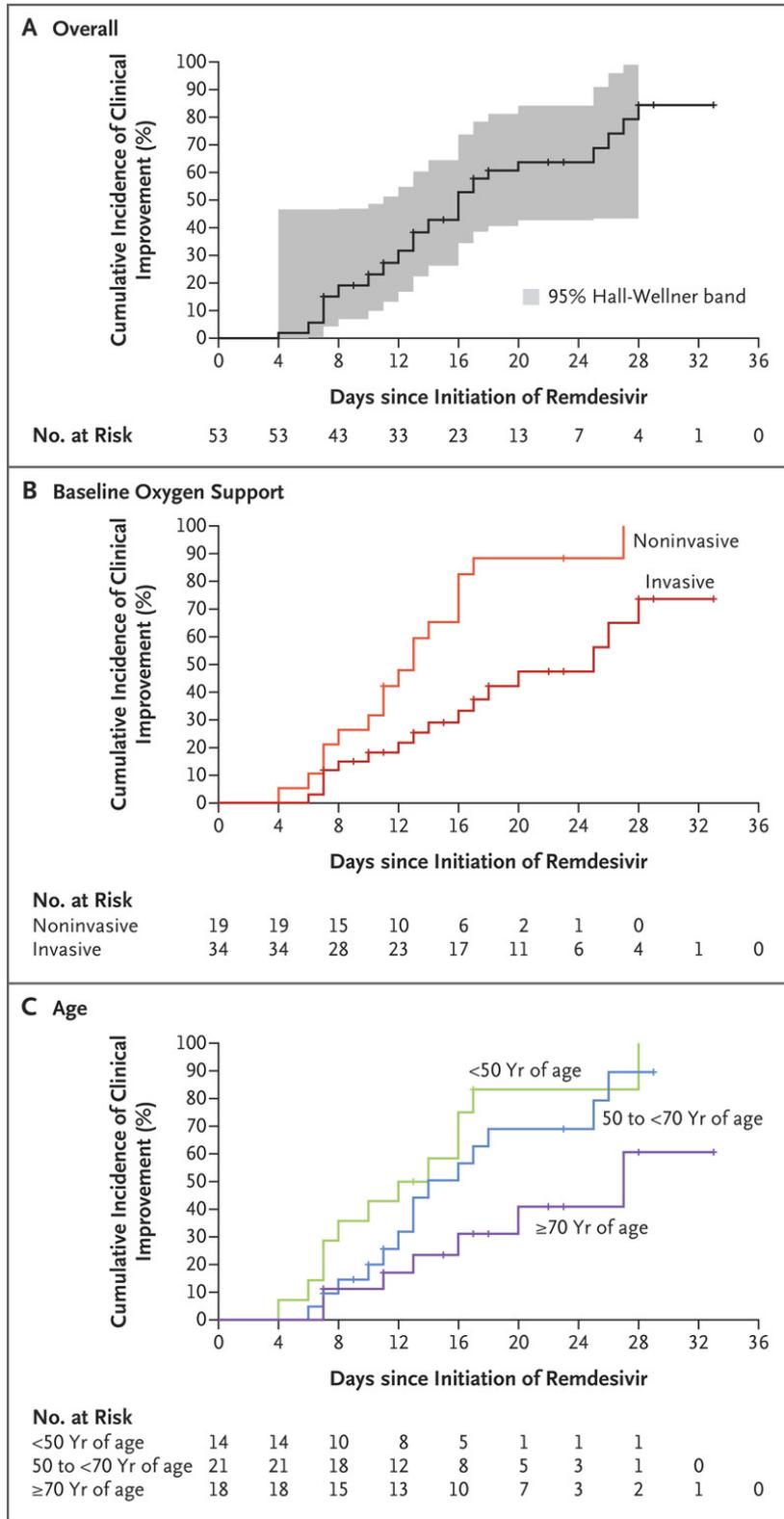
Figure 2.



Changes in Oxygen-Support Status from Baseline in Individual Patients.

Over a median follow-up of 18 days (interquartile range, 13 to 23) after receiving the first dose of remdesivir, 36 of 53 patients (68%) showed an improvement in the category of oxygen support, whereas 8 of 53 patients (15%) showed worsening (Figure 1). Improvement was observed in all 12 patients who were breathing ambient air or receiving low-flow supplemental oxygen and in 5 of 7 patients (71%) who were receiving noninvasive oxygen support (NIPPV or high-flow supplemental oxygen). It is notable that 17 of 30 patients (57%) who were receiving invasive mechanical ventilation were extubated, and 3 of 4 patients (75%) receiving ECMO stopped receiving it; all were alive at last follow-up. Individual patients' changes in the category of oxygen support are shown in Figure 2. By the date of the most recent follow-up, 25 of 53 patients (47%) had been discharged (24% receiving invasive ventilation [8 of 34 patients] and 89% [17 of 19 patients] receiving noninvasive oxygen support).

Figure 3.



Cumulative Incidence of Clinical Improvement from Baseline to Day 36.

By 28 days of follow-up, the cumulative incidence of clinical improvement, as defined by either a decrease of 2 points or more on the six-point ordinal scale or live discharge, was 84% (95% confidence interval [CI], 70 to 99) by Kaplan–Meier analysis (Figure 3A). Clinical improvement was less frequent among patients receiving invasive ventilation than among those receiving

noninvasive ventilation (hazard ratio for improvement, 0.33; 95% CI, 0.16 to 0.68) (Figure 3B) and among patients 70 years of age or older (hazard ratio as compared with patients younger than 50 years, 0.29; 95% CI, 0.11 to 0.74) (Figure 3C). Sex, region of enrollment, coexisting conditions, and duration of symptoms before remdesivir treatment was initiated were not significantly associated with clinical improvement (Table S1).

MORTALITY

Seven of the 53 patients (13%) died after the completion of remdesivir treatment, including 6 of 34 patients (18%) who were receiving invasive ventilation and 1 of 19 (5%) who were receiving noninvasive oxygen support (see the [Supplementary Appendix](#) for case narratives). The median interval between remdesivir initiation and death was 15 days (interquartile range, 9 to 17).

Overall mortality from the date of admission was 0.56 per 100 hospitalization days (95% CI, 0.14 to 0.97) and did not differ substantially among patients receiving invasive ventilation (0.57 per 100 hospitalization days; 95% CI, 0 to 1.2]) as compared with those receiving noninvasive ventilation (0.51 per 100 hospitalization days; 95% CI, 0.07 to 1.1]). Risk of death was greater among patients who were 70 years of age or older (hazard ratio as compared with patients younger than 70 years, 11.34; 95% CI, 1.36 to 94.17) and among those with higher serum creatinine at baseline (hazard ratio per milligram per deciliter, 1.91; 95% CI, 1.22 to 2.99). The hazard ratio for patients receiving invasive ventilation as compared with those receiving noninvasive oxygen support was 2.78 (95% CI, 0.33 to 23.19) (Table S2).

SAFETY

Table 2.

Table 2. Summary of Adverse Events.

Event	Invasive Ventilation (N=34)	Noninvasive Oxygen Support (N=19)	Total (N=53)
	number of patients (percent)		
Any adverse event	22 (65)	10 (53)	32 (60)
Adverse events occurring in 2 or more patients			
Hepatic enzyme increased*	8 (24)	4 (21)	12 (23)
Diarrhea	1 (3)	4 (21)	5 (9)
Rash	3 (9)	1 (5)	4 (8)
Renal impairment	4 (12)	0	4 (8)
Hypotension	3 (9)	1 (5)	4 (8)
Acute kidney injury	2 (6)	1 (5)	3 (6)
Atrial fibrillation	2 (6)	1 (5)	3 (6)
Multiple-organ-dysfunction syndrome	3 (9)	0	3 (6)
Hypernatremia	3 (9)	0	3 (6)
Deep-vein thrombosis	3 (9)	0	3 (6)
Acute respiratory distress syndrome	1 (3)	1 (5)	2 (4)
Pneumothorax	2 (6)	0	2 (4)
Hematuria	2 (6)	0	2 (4)
Delirium	1 (3)	1 (5)	2 (4)
Septic shock	2 (6)	0	2 (4)
Pyrexia	1 (3)	1 (5)	2 (4)
Any serious adverse event	9 (26)	3 (16)	12 (23)
Serious events occurring in 2 or more patients			
Multiple-organ-dysfunction syndrome	2 (6)	0	2 (4)
Septic shock	2 (6)	0	2 (4)
Acute kidney injury	2 (6)	0	2 (4)
Hypotension	2 (6)	0	2 (4)

* Adverse-event terms are based on the *Medical Dictionary for Regulatory Activities*, version 22.1. Hepatic enzyme increased includes the following terms: hepatic enzyme increased, alanine aminotransferase increased, aspartate aminotransferase increased, and transaminases increased. Elevated hepatic enzymes resulted in discontinuation of remdesivir therapy in 2 patients.

Summary of Adverse Events.

A total of 32 patients (60%) reported adverse events during follow-up (Table 2). The most common adverse events were increased hepatic enzymes, diarrhea, rash, renal impairment, and hypotension. In general, adverse events were more common in patients receiving invasive ventilation. A total of 12 patients (23%) had serious adverse events. The most common serious adverse events — multiple-organ-dysfunction syndrome, septic shock, acute kidney injury, and hypotension — were reported in patients who were receiving invasive ventilation at baseline.

Four patients (8%) discontinued remdesivir treatment prematurely: one because of worsening of preexisting renal failure, one because of multiple organ failure, and two because of elevated aminotransferases, including one patient with a maculopapular rash.

LABORATORY DATA

Given the nature of this compassionate-use program, data on a limited number of laboratory measures were collected. Median serum ALT, AST, and creatinine fluctuated during follow-up (Fig. S2).

Discussion



To date, no therapy has demonstrated efficacy for patients with Covid-19. This preliminary report describes the clinical outcomes in a small cohort of patients who were severely ill with Covid-19 and were treated with remdesivir. Although data from several ongoing randomized, controlled trials will soon provide more informative evidence regarding the safety and efficacy of remdesivir for Covid-19, the outcomes observed in this compassionate-use program are the best currently available data. Specifically, improvement in oxygen-support status was observed in 68% of patients, and overall mortality was 13% over a median follow-up of 18 days. In a recent randomized, controlled trial of lopinavir–ritonavir in patients hospitalized for Covid-19, the 28-day mortality was 22%.¹⁰ It is important to note that only 1 of 199 patients in that trial were receiving invasive ventilation at baseline. In case series and cohort studies, largely from China, mortality rates of 17 to 78% have been reported in severe cases, defined by the need for admission to an intensive care unit, invasive ventilation, or both.²³⁻²⁸ For example, among 201 patients hospitalized in Wuhan, China, mortality was 22% overall and 66% (44 of 67) among patients receiving invasive mechanical ventilation.⁷ By way of comparison, the 13% mortality observed in this remdesivir compassionate-use cohort is noteworthy, considering the severity of disease in this patient population; however, the patients enrolled in this compassionate-treatment program are not directly comparable to those studied in these other reports. For example, 64% of remdesivir-treated patients were receiving invasive ventilation at baseline, including 8% who were receiving ECMO, and mortality in this subgroup was 18% (as compared with 5.3% in patients receiving noninvasive oxygen support), and the majority (75%) of patients were male, were over 60 years of age, and had coexisting conditions.

Unfortunately, our compassionate-use program did not collect viral load data to confirm the antiviral effects of remdesivir or any association between baseline viral load and viral suppression, if any, and clinical response. Moreover, the duration of remdesivir therapy was not entirely uniform in our study, largely because clinical improvement enabled discharge from the hospital. The effectiveness of a shorter duration of therapy (e.g., 5 days, as compared with 10 days), which would allow the treatment of more patients during the pandemic, is being assessed in ongoing randomized trials of this therapy.

No new safety signals were detected during short-term remdesivir therapy in this compassionate-use cohort. Nonclinical toxicology studies have shown renal abnormalities, but no clear evidence of nephrotoxicity due to remdesivir therapy was observed. As reported in studies in healthy volunteers and patients infected with Ebola virus, mild-to-moderate

elevations in ALT, AST, or both were observed in this cohort of patients with severe Covid-19.^{18,19} However, considering the frequency of liver dysfunction in patients with Covid-19, attribution of hepatotoxicity to either remdesivir or the underlying disease is challenging.²⁹ Nevertheless, the safety and side-effect profile of remdesivir in patients with Covid-19 require proper assessment in placebo-controlled trials.

Interpretation of the results of this study is limited by the small size of the cohort, the relatively short duration of follow-up, potential missing data owing to the nature of the program, the lack of information on 8 of the patients initially treated, and the lack of a randomized control group. Although the latter precludes definitive conclusions, comparisons with contemporaneous cohorts from the literature, in whom general care is expected to be consistent with that of our cohort, suggest that remdesivir may have clinical benefit in patients with severe Covid-19. Nevertheless, other factors may have contributed to differences in outcomes, including the type of supportive care (e.g., concomitant medications or variations in ventilatory practices) and differences in institutional treatment protocols and thresholds for hospitalization. Moreover, the use of invasive ventilation as a proxy for disease severity may be influenced by the availability of ventilators in a given location. The findings from these uncontrolled data will be informed by the ongoing randomized, placebo-controlled trials of remdesivir therapy for Covid-19.

Funding and Disclosures

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[Disclosure forms](#) provided by the authors are available with the full text of this article at [NEJM.org](https://www.nejm.org).

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Supplementary Material



Protocol	PDF	286KB
Supplementary Appendix	PDF	1572KB
Disclosure Forms	PDF	824KB

References (29) ▼

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed* 2020;91:157-160.
[Medline](#) | [Google Scholar](#)

2. Spinelli A, Pellino G. COVID-19 pandemic: perspectives on an unfolding crisis. *Br J Surg* 2020 March 19 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)

3. Fauci AS, Lane HC, Redfield RR. Covid-19 — navigating the uncharted. *N Engl J Med* 2020;382:1268-1269.
[Free Full Text](#) | [Medline](#) | [Google Scholar](#)

4. Mahase E, Kmiotowicz Z. Covid-19: doctors are told not to perform CPR on patients in cardiac arrest. *BMJ* 2020;368:m1282-m1282.
[Crossref](#) | [Medline](#) | [Google Scholar](#)

5. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis* 2020 March 13 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)

6. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. *Lancet* 2020;395:1014-1015.
[Crossref](#) | [Medline](#) | [Google Scholar](#)

7. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020 March 13 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)

8. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020 March 23 (Epub ahead of print).

9. Poston JT, Patel BK, Davis AM. Management of critically ill adults with COVID-19. JAMA 2020 March 26 (Epub ahead of print).

[Crossref](#) | [Web of Science](#) | [Medline](#) | [Google Scholar](#)

10. Cao B, Wang Y, Wen D, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2001282.

[Free Full Text](#) | [Google Scholar](#)

11. Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020 March 27 (Epub ahead of print).

[Crossref](#) | [Medline](#) | [Google Scholar](#)

12. Touret F, de Lamballerie X. Of chloroquine and COVID-19. Antiviral Res 2020 March 5 (Epub ahead of print).

[Crossref](#) | [Medline](#) | [Google Scholar](#)

13. Baden LR, Rubin EJ. Covid-19 — the search for effective therapy. N Engl J Med. DOI: 10.1056/NEJMe2005477.

[Free Full Text](#) | [Google Scholar](#)

14. de Wit E, Feldmann F, Cronin J, et al. Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. Proc Natl Acad Sci U S A 2020;117:6771-6776.

[Crossref](#) | [Web of Science](#) | [Medline](#) | [Google Scholar](#)

15. Sheahan TP, Sims AC, Graham RL, et al. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Sci Transl Med 2017;9(396):eaal3653-eaal3653.

[Crossref](#) | [Web of Science](#) | [Medline](#) | [Google Scholar](#)

16. Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun 2020;11:222-222.

[Crossref](#) | [Medline](#) | [Google Scholar](#)

-
- 17.** Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 2020;30:269-271.
[Crossref](#) | [Web of Science](#) | [Medline](#) | [Google Scholar](#)
-
- 18.** Mulangu S, Dodd LE, Davey RT Jr, et al. A randomized, controlled trial of Ebola virus disease therapeutics. *N Engl J Med* 2019;381:2293-2303.
[Free Full Text](#) | [Web of Science](#) | [Medline](#) | [Google Scholar](#)
-
- 19.** European Medicines Agency. Summary on compassionate use: Remdesivir Gilead. April 3, 2020 (https://www.ema.europa.eu/en/documents/other/summary-compassionate-use-remdesivir-gilead_en.pdf).
[Google Scholar](#)
-
- 20.** Kujawski SA, Wong KK, Collins JP, et al. First 12 patients with coronavirus disease 2019 (COVID-19) in the United States. medRxiv, March 12, 2020 (<https://www.medrxiv.org/content/10.1101/2020.03.09.20032896v1>).
[Google Scholar](#)
-
- 21.** Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020;382:929-936.
[Free Full Text](#) | [Web of Science](#) | [Medline](#) | [Google Scholar](#)
-
- 22.** Lescure FX, Bouadma L, Nguyen D, et al. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. *Lancet Infect Dis* 2020 March 27 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)
-
- 23.** Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA* 2020 March 19 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)
-
- 24.** Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020 February 7 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)
-

25. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72@ 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020 February 24 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)

26. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-1062.
[Crossref](#) | [Medline](#) | [Google Scholar](#)

27. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region — case series. N Engl J Med. DOI: 10.1056/NEJMoa2004500.
[Free Full Text](#) | [Google Scholar](#)

28. ICNARC report on COVID-19 in critical care. London: Intensive Care National Audit & Research Centre, March 27, 2020
(<https://www.icnarc.org/DataServices/Attachments/Download/b5f59585-5870-ea11-9124-00505601089b>).
[Google Scholar](#)

29. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol 2020 March 4 (Epub ahead of print).
[Crossref](#) | [Medline](#) | [Google Scholar](#)

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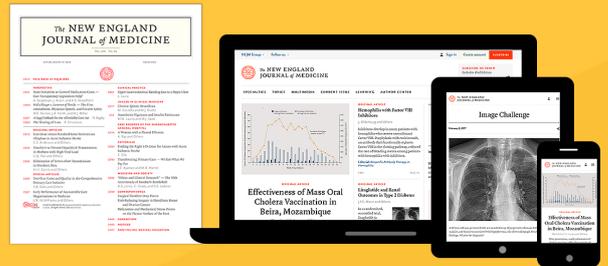
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