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MAJOR ARTICLE

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection: An Analysis of 28-Day Mortality

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Background. Remdesivir is approved by the US Food and Drug Administration for the treatment of patients hospitalized with coronavirus disease 2019 (COVID-19) and has been shown to shorten time to recovery and improve clinical outcomes in randomized trials.

Methods. This was the final day 28 comparative analysis of data from a phase 3, randomized, open-label study comparing 2 remdesivir regimens (5 vs 10 days, combined for this analysis [remdesivir cohort]) and a real-world retrospective longitudinal cohort study of patients receiving standard-of-care treatment (nonremdesivir cohort). Eligible patients, aged ≥18 years, had confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), oxygen saturation ≤94% on room air or required supplemental oxygen, with pulmonary infiltrates. Propensity score matching (up to 1:10 ratio) was used to ensure comparable populations. We assessed day 14 clinical recovery (determined using a 7-point ordinal scale) and day 28 all-cause mortality (coprimary endpoints).

Results. A total of 368 (remdesivir) and 1399 (nonremdesivir) patients were included in the matched analysis. The day 14 clinical recovery rate was significantly higher among the remdesivir versus the nonremdesivir cohort (65.2% vs 57.1%; odds ratio [OR], 1.49; 95% confidence interval [CI], 1.16–1.90; $P = 0.002$). The day 28 mortality rate was significantly lower in the remdesivir cohort versus the nonremdesivir cohort (12.0% vs 16.2%; OR, 0.67; 95% CI, 0.47–.95; $P = .03$).

Conclusions. Remdesivir was associated with significantly higher rates of day 14 clinical recovery, and lower day 28 mortality, compared with standard-of-care treatment in hospitalized patients with COVID-19. These data, taken together, support the use of remdesivir to improve clinical recovery and decrease mortality from SARS-CoV-2 infection.

Keywords. COVID-19; mortality; remdesivir; SARS-CoV-2.

The impact of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) global pandemic has been, and continues to be, significant [1]. Morbidity and mortality are considerable among older adults and those with comorbidities [2]. There has been an unprecedented global effort to develop strategies against SARS-CoV-2 infection, with ongoing trials assessing antiviral, anti-inflammatory, and immunomodulatory treatments to be used alongside public health measures [3]. Efforts to identify effective treatments to complement accelerating vaccination programs remain a public health priority [4].

Remdesivir is a direct-acting nucleotide-analog prodrug that inhibits *Coronaviridae* ribonucleic acid (RNA)-dependent RNA polymerase through incorporation of its triphosphate form into the viral RNA [5]. Remdesivir inhibits SARS-CoV-2 replication in vitro [6, 7], and accumulating clinical evidence supports its use in patients with moderate or severe SARS-CoV-2 infection [8–12]. Data from a double-blind, randomized controlled trial indicated a reduced time to recovery in patients hospitalized with SARS-CoV-2 infection receiving intravenous remdesivir for 10 days compared with placebo (median time to recovery 10 days [95% confidence interval {CI}, 9–11 days] vs 15 days [95% CI, 13–18 days]) [11]. Remdesivir was approved by the US Food and Drug Administration for use in hospitalized adults

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and pediatric patients (≥12 years and weighing ≥40 kg) with SARS-CoV-2 infection and received conditional marketing authorization from the European Medicines Agency for use in patients with SARS-CoV-2-related pneumonia receiving supplemental oxygen.

The efficacy of remdesivir in patients with severe SARS-CoV-2 infection was recently assessed in a comparative analysis of data from 2 studies: (1) a prospective phase 3, placebo-controlled, randomized study of remdesivir [8] and (2) a real-world retrospective cohort study of patients receiving standard-of-care therapy [13]. In an interim analysis, day 14 clinical recovery (based on improvement on a 7-point ordinal scale) was reported in 74.4% of patients in the remdesivir cohort compared with 59.0% in the nonremdesivir cohort (adjusted odds ratio [OR], 2.03; 95% CI, 1.34–3.08; $P < .001$) [13]. The secondary endpoint of day 14 mortality was lower in the remdesivir cohort versus the nonremdesivir cohort (7.6% vs 12.5%; adjusted OR, 0.38; 95% CI, 0.22–0.68; $P = .001$) [13]. In the final analysis, presented herein, after accrual of additional patients to allow for propensity matching, we describe the final results of this comparative study, the coprimary endpoints of day 14 clinical recovery, and day 28 all-cause mortality.

METHODS

The study design, patient populations, and endpoints from this comparative analysis have been described previously [13]. The prospective Study 5773 (Clinical trial: NCT04292899/GS-US-540-5773) is a phase 3, randomized, open-label study conducted at 55 sites in the United States, Europe, and Asia [8]. The retrospective Study 5807 (Clinical trial: EUPAS34303/GS-US-540-5807) was a real-world longitudinal cohort study conducted at 32 sites in the United States, Europe, and Asia.

Patient Consent Statement

In prospective Study 5773, the protocol was approved by local institutional review boards or independent ethics committees, and the study was conducted in accordance with the principles of the Declaration of Helsinki and International Conference on Harmonisation Good Clinical Practice guidelines. In Study 5773, patients or their legally authorized representative provided written informed consent or assent. Retrospective Study 5807 was conducted in compliance with Good Pharmacoepidemiology and Good Pharmacovigilance Practice. In Study 5807, patients or their legally authorized representative provided written informed consent or assent for the use of deidentified secondary data as appropriate and when required by the regulations of the individual Institutional Review Boards.

Patients

The inclusion criteria for patient enrollment in Study 5807 were designed to align with those in Study 5773 (described previously [8, 13]). Both studies enrolled patients with SARS-CoV-2 infection confirmed by polymerase chain reaction who had oxygen saturation ≤94% on room air or required supplemental oxygen and with radiographically confirmed pulmonary infiltrates (ie, patients with severe coronavirus disease 2019 [COVID-19]). Only patients aged ≥18 years were included in the current analysis.

To ensure comparability of patient populations, the exclusion criteria for prospective Study 5773 were retroactively applied to the retrospective Study 5807 population. Thus, patients were excluded from both studies if they had venoarterial extracorporeal membrane oxygenation on day 1; alanine transferase or aspartate transferase >5 × upper limit of normal; creatinine clearance <50 mL/min (Cockcroft-Gault formula); or were pregnant or breastfeeding. Patients were excluded from prospective Study 5773 if they were receiving medication for the treatment of SARS-CoV-2 infection or mechanical ventilation at screening; however, patients enrolled in retrospective Study 5807 were allowed to receive treatments for SARS-CoV-2 infection, excluding remdesivir. Between the interim and final analyses, an additional 2074 patients were enrolled in retrospective Study 5807 (including patients in Spain/Italy, data from which were not available for the interim analysis) to allow for the propensity-matched analysis.

Treatment

In prospective Study 5773, patients were randomized 1:1 to receive open-label remdesivir 200 mg on day 1 followed by remdesivir 100 mg/day either on days 2–5 or on days 2–10 (randomization was 5 vs 10 days). All patients also received standard-of-care treatment (determined by local site practice). In the primary analysis of Study 5773, there was no significant difference in efficacy or safety outcomes according to remdesivir treatment duration, and therefore data from both treatment arms were pooled for this comparative analysis [8]. In retrospective Study 5807, all patients received standard-of-care treatment (nonremdesivir cohort) as determined by local treatment practices (except remdesivir, which was not approved for routine clinical use at the time of study).

Endpoints

The coprimary endpoints for retrospective Study 5807 final analysis were day 14 clinical recovery after initiation of treatment and day 28 all-cause mortality. Clinical status was determined using a 7-point ordinal scale as previously described [13] (Table 1).

An earlier preplanned interim analysis reported change in day 14 clinical status (recovery) in the remdesivir and nonremdesivir cohorts and day 14 mortality rates [13]. The present report documents the final analysis based on completed data collection from additional patients and full 28-day follow-up.

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Statistical Analysis

Propensity score matching was used to form matched sets of patients from treated and control populations with similar propensity scores; no imputation was used in this analysis. Propensity scores were calculated using a logistic regression model to determine the probability of treatment assignment based on observed baseline characteristics as independent variables and treatment assignment (remdesivir vs no remdesivir) as the dependent variable. Baseline was defined as the start of remdesivir therapy in prospective Study 5773 and the date of hospitalization in retrospective Study 5807. Baseline factors included in the propensity score model are summarized in Table 2. See Supplementary Methods for further information on the propensity score matching. Recruitment for both studies was conducted before the results of the RECOVERY trial [14] and before the adoption of dexamethasone as part of standard of care in the clinic; thus, data on corticosteroid use were not collected in Study 5807.

For the primary analysis, recovery and mortality rates were analyzed using a generalized estimating equation (GEE) logistic regression model including treatment as an independent variable and matched sets as clusters [15]. Additional analyses evaluated factors associated with day 28 mortality using a multivariable GEE logistic regression model; covariates used in the model are listed in Table 2.

A subgroup analysis of patients categorized according to oxygen support status required at baseline (based on the 7-point ordinal scale) was conducted. The patient subgroups included those on invasive mechanical ventilation, high-flow oxygen (>6 L/min), low-flow oxygen (≤6 L/min), or room air (no supplemental oxygen required). SAS version 9.4 (SAS Institute Inc., Cary, NC) was used.

RESULTS

Patients

The first patient's initial visit in Study 5773 was on March 6, 2020 and the last patient's last visit was on April 27, 2020. The first patient enrolled in Study 5807 was hospitalized on February 6, 2020; data collection for Study 5807 was completed on May 15, 2020.

Of 397 patients who received remdesivir in Study 5773, 368 were included in the final analysis set (remdesivir cohort), whereas 1399 (from 2710 available before matching) were included from Study 5807 (nonremdesivir cohort) (Supplementary Figure 1).

After matching, a notable difference between remdesivir and nonremdesivir cohorts was the receipt of medications for COVID-19 treatment (Supplementary Table 1). Before baseline, azithromycin use was higher in the remdesivir than nonremdesivir cohort (32.3% vs 19.0%). After matching, the factors used for the propensity score matching were generally well balanced. Table 3 summarizes baseline demographics and disease characteristics in the matched populations. Both cohorts were broadly similar in terms of sex, age, race, and region of enrollment (Table 3). Comorbidities were also similar between treatment groups.

Coprimary Analyses: Day 14 Clinical Recovery and Day 28 Mortality

The day 14 clinical recovery rate was significantly higher in the remdesivir than nonremdesivir cohort (65.2% vs 57.1%; OR, 1.49; 95% CI, 1.16–1.90; $P = .002$) (Figure 1A). Day 28 mortality was statistically significantly lower in the remdesivir than nonremdesivir cohort: 44 of 368 patients in the remdesivir cohort and 226 of 1399 in the nonremdesivir cohort had died (12.0% vs 16.2%; OR, 0.67; 95% CI, 0.47–0.95; $P = .03$) (Figure 1B).

Subgroup and Multivariable Mortality Analyses

Day 14 recovery and day 28 mortality were evaluated after stratification for baseline oxygen requirement (Figure 2). The recovery rate was significantly higher for remdesivir-treated patients on low-flow oxygen at baseline compared with the nonremdesivir cohort on low-flow oxygen, 78.6% versus 65.7%, respectively (OR, 2.00; 95% CI, 1.38–2.90; $P = .0002$). The mortality rate was significantly lower for

Table 1. Ordinal Scale and Recovery Criteria[a]

Ordinal Scale	
1	Death
2	Hospitalized and receiving invasive mechanical ventilation or ECMO
3	Hospitalized and receiving noninvasive ventilation or high-flow oxygen
4	Hospitalized and requiring low-flow supplemental oxygen
5	Hospitalized and not requiring supplemental oxygen but receiving ongoing medical care
6	Hospitalized and not requiring supplemental oxygen or ongoing medical care
7	Not hospitalized
Recovery	
Recovery was defined as a change in ordinal scale: from 2–4 to 5–7; or from 5 to 6–7; or from 6 to 7	

Abbreviations: ECMO, extracorporeal membrane oxygenation.

[a]The ordinal scale was a modified version from that used by Cao et al [36] and that proposed in the draft WHO R&D Blueprint COVID-19 Therapeutic Trial Synopsis [37]. If an ongoing hospitalized patient had missing clinical status at a visit, then the last available post-baseline clinical status before the visit with the missing value was used for that visit.

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Table 2. Baseline Factors Included in the Propensity Score Model[a]

Duration of symptoms before baseline
Clinical status using the 7-point ordinal scale score
Age (<40 years, 40–64 years, and ≥65 years)
Sex
Race (Asian, black, other, and white)
Country of enrollment (Italy, Spain, United States, other)
Obesity
Comorbidities (hypertension, cardiovascular disease, diabetes mellitus, COPD, asthma)
Investigational COVID-19 medications at the time of study design (azithromycin, biologics, HIV protease inhibitors, hydroxychloroquine, ribavirin[b]) taken at/before baseline

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus.

[a]Baseline factors included in the propensity score model incorporated some of the sociodemographic factors and comorbidities outlined by the Centers for Disease Control and Prevention that may affect risk of severe illness [38].

[b]Ribavirin was not included in the multivariable generalized estimating equation logistic regression model because the numbers were too low.

remdesivir-treated patients on low-flow oxygen at baseline compared with the nonremdesivir cohort on low-flow oxygen, 4.3% versus 12.5%, respectively (OR, 0.29; 95% CI, 0.14–0.58; $P = .0005$). No significant differences in recovery or mortality were identified between both cohorts for patients who were on room air or high-flow oxygen. No recovery or mortality benefit was apparent for patients on mechanical ventilation at baseline, although the number of patients in this subgroup was small.

To evaluate additional factors influencing survival, a multivariable analysis that included remdesivir treatment and other factors associated with COVID-19 outcomes was performed. In the multivariable analysis, the OR for death by day 28, comparing the remdesivir versus nonremdesivir cohort, was similar to the primary analysis (OR, 0.65; 95% CI, 0.44–0.96; $P = .03$) (Figure 3). This demonstrates that remdesivir treatment reduces mortality after accounting for all the factors included in the model. In addition (again, accounting for all the other factors in the model), a lower risk of death was associated with longer duration of symptoms before baseline, younger age, female sex, white race/ethnicity (vs black/African American), receiving a human immunodeficiency virus (HIV) protease inhibitor before or at baseline (where baseline was the start of remdesivir or date of hospitalization), not having cardiovascular disease or chronic obstructive pulmonary disease, and being on room air or low-flow oxygen at baseline (vs invasive mechanical ventilation).

DISCUSSION

Treatment with remdesivir was associated with a significant reduction in the rate of day 28 all-cause mortality compared with standard-of-care treatment in patients hospitalized with COVID-19. In addition, the day 14 clinical recovery rate was significantly higher in the remdesivir cohort. Because surges in SARS-CoV-2 infections have pushed healthcare systems to the limits of their capacity in some countries, a beneficial effect of remdesivir treatment in shortening clinical recovery times could ease the burden on hospitals.

These findings represent the final analysis of a previously reported interim analysis [13]. There are several important differences between the analyses. The present analysis used an increased population size in both the remdesivir and nonremdesivir groups, including >500 additional patients in the nonremdesivir cohort (818 in the interim/1399 in the final). The interim analysis used inverse probability of treatment weighting, because sample size in the nonremdesivir cohort was insufficient for matching (at time of analysis). The final analysis included sufficient nonremdesivir patients to enable propensity score matching. Propensity score matching was able to balance baseline covariates and ensure comparable populations regarding characteristics that might influence clinical outcome. In addition, patients from Italy and Spain were included in this analysis, further increasing global representation and generalizability (data unavailable for these patients at interim analysis). With the increased sample size and inclusion of additional patients from Europe, the day 28 mortality benefit and the day 14 clinical recovery benefit were confirmed (coprimary endpoints).

Several studies have evaluated remdesivir for COVID-19. In our study, we found a clear mortality benefit with remdesivir, but randomized trials have not demonstrated this. A randomized clinical trial conducted in China failed to identify a statistically significant difference in time to clinical improvement with remdesivir versus placebo in patients with severe COVID-19 (hazard ratio [HR], 1.23; 95% CI, 0.87–1.75) [12]. Day 28 mortality was also not different between arms in that study (HR, 1.1; 95% CI, −0.81 to 10.3). Notably, that study was underpowered due to poor enrollment and early study closure [16]. The ACTT-1 study compared remdesivir (200 mg loading dose followed by 100 mg daily for up to 9 additional days) with placebo in adults hospitalized with COVID-19 with evidence of lower respiratory tract infection [11]. Patients receiving remdesivir had a shorter time to recovery (defined as meeting the criteria

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Table 3. Patient Demographics and Baseline Characteristics for the Matched Population (Based on Propensity Match Scoring) (Full Analysis Set)

Characteristic	Remdesivir Cohort (*n* = 368)	Nonremdesivir Cohort (*n* = 1399[a])
Sex, *n* (%)		
Male	231 (62.8)	877 (62.7)
Female	137 (37.2)	522 (37.3)
Age, mean (SD), years	59.7 (14.7)	60.5 (14.8)
Age range, *n* (%)		
<40 years	38 (10.3)	141 (10.1)
40–64 years	178 (48.4)	683 (48.9)
≥65 years	152 (41.3)	574 (41.1)
Race		
White	251 (68.2)	949 (67.9)
Asian	42 (11.4)	164 (11.7)
Black or African American	43 (11.7)	171 (12.2)
Other	32 (8.7)	115 (8.3)
Region		
United States	218 (59.2)	820 (58.6)
Italy	66 (17.9)	247 (17.6)
Spain	55 (15.0)	221 (15.8)
Other	29 (7.9)	111 (7.9)
BMI, *n* (%)		
<30 kg/m^2	210 (57.1)	821 (58.7)
≥30 kg/m^2	158 (42.9)	578 (41.4)
Comorbidities, *n* (%)		
Hypertension	183 (49.7)	692 (49.5)
Cardiovascular disease	103 (28.0)	365 (26.1)
Diabetes mellitus	85 (23.1)	325 (23.2)
Chronic obstructive pulmonary disease	17 (4.6)	71 (5.1)
Asthma	46 (12.5)	181 (13.0)
Medications With Potential Activity Against COVID-19 Taken Before or at Baseline[b], *n* (%)		
Azithromycin	119 (32.3)	426 (30.5)
Biologics[c]	16 (4.4)	52 (3.7)
HIV protease inhibitor	36 (9.8)	139 (10.0)
Hydroxychloroquine group[d]	88 (23.9)	336 (24.0)
Ribavirin	2 (0.5)	6 (0.4)
Baseline[b] Clinical Status on 7-Point Ordinal Scale[e]		
2	12 (3.3)	48 (3.4)
3	94 (25.5)	351 (25.1)
4	210 (57.1)	803 (57.4)
5	52 (14.1)	197 (14.1)
Duration of symptoms, mean (SD), days	9.1 (3.8)	8.9 (5.7)
Baseline[b] ALT, mean (SD), U/L	43.0 (31.8)	42.5 (31.2) [*n* = 1274]
Baseline[b] AST, mean (SD), U/L	50.7 (28.7) [*n* = 362]	49.0 (28.8) [*n* = 1188]
eGFR, mean (SD), mL/min	114.3 (48.8)	103.9 (41.7) [*n* = 1267]

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; HIV, human immunodeficiency virus; SD, standard deviation.

[a]Weighted summary statistics.

[b]Defined as the start of remdesivir therapy in prospective Study 5773 (remdesivir cohort) and the date of hospitalization in retrospective Study 5807 (nonremdesivir cohort).

[c]Biologics included interferons, investigational biologics, plasma, sarilumab, siltuximab, and tocilizumab.

[d]Hydroxychloroquine group included aminoquinolines, chloroquine, hydroxychloroquine, and hydroxychloroquine sulfate.

[e]2 = hospitalized and receiving invasive mechanical ventilation or extracorporeal membrane oxygenation; 3 = hospitalized and receiving noninvasive ventilation or high-flow oxygen; 4 = hospitalized and requiring low-flow supplemental oxygen; 5 = hospitalized and not requiring supplemental oxygen but receiving ongoing medical care.

for the top 3 categories on an 8-point ordinal scale) compared with those receiving placebo (median time to recovery, 10 [95% CI, 9–11] vs 15 [95% CI, 13–18] days; rate ratio for recovery, 1.29 [95% CI, 1.12–1.49]; $P < .001$) [11]. In addition, patients receiving remdesivir were more likely to have clinical improvement at day 15 than those receiving placebo (OR, 1.5, 95% CI, 1.2–1.9, after adjustment for disease severity). Consistent with the findings of the present analysis, Kaplan-Meier mortality estimates with remdesivir versus placebo were 6.7% versus 11.9% at day 15 (HR, 0.55; 95% CI, 0.36–0.83) and

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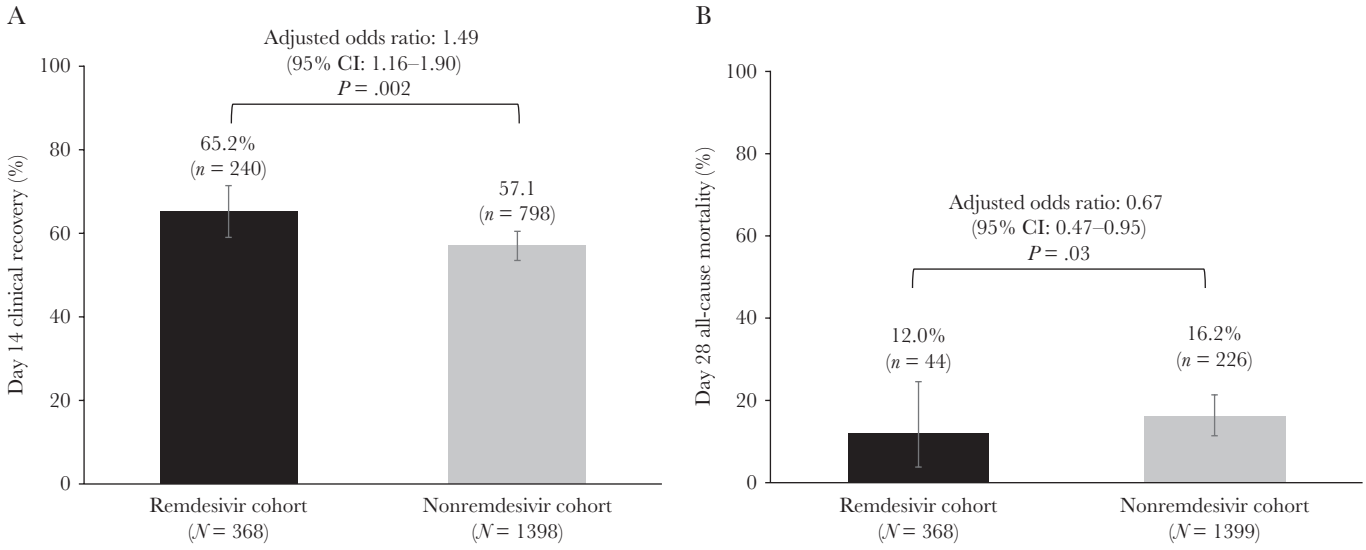

Figure 1. Primary endpoint analyses: (A) odds ratio for day 14 clinical recovery; (B) odds ratio for day 28 all-cause mortality. *P* value, odds ratio, and 95% confidence interval (CI) were based on the generalized estimating equation logistic regression with propensity-matched sets considered as clusters. Numbers for the nonremdesivir cohort are based on weighted statistics.

11.4% versus 15.2% at day 29 (HR, 0.73; 95% CI, 0.52–1.03). The benefit of remdesivir was most apparent in patients receiving low-flow oxygen—consistent with the results of our subgroup analysis, which demonstrated a highly significant recovery and

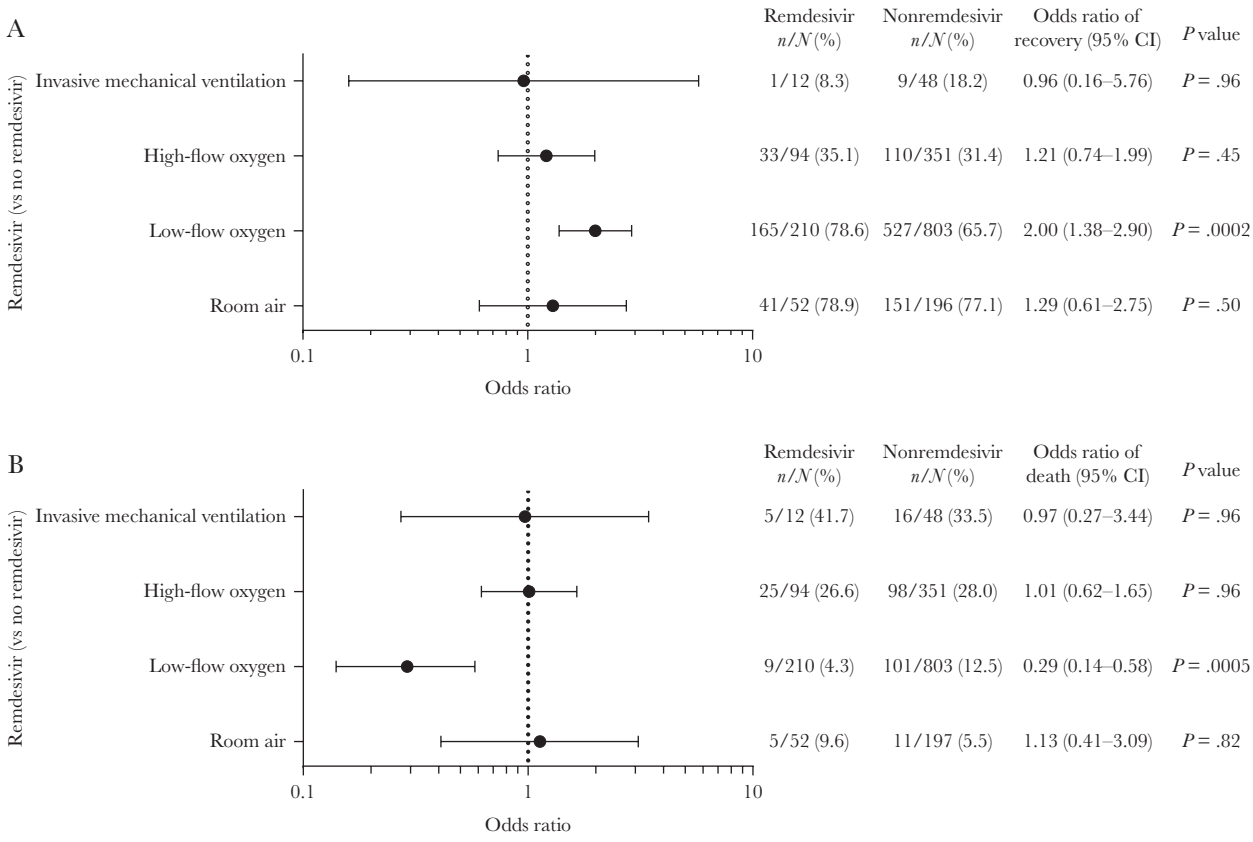

Figure 2. Subgroup analysis of patients categorized according to oxygen support status required at baseline (based on propensity score matching) for (A) day 14 recovery and (B) day 28 all-cause mortality. *P* value, odds ratio, and 95% confidence interval (CI) were based on the generalized estimating equation logistic regression with matched sets considered as clusters. Numbers for the nonremdesivir cohort are based on weighted statistics.

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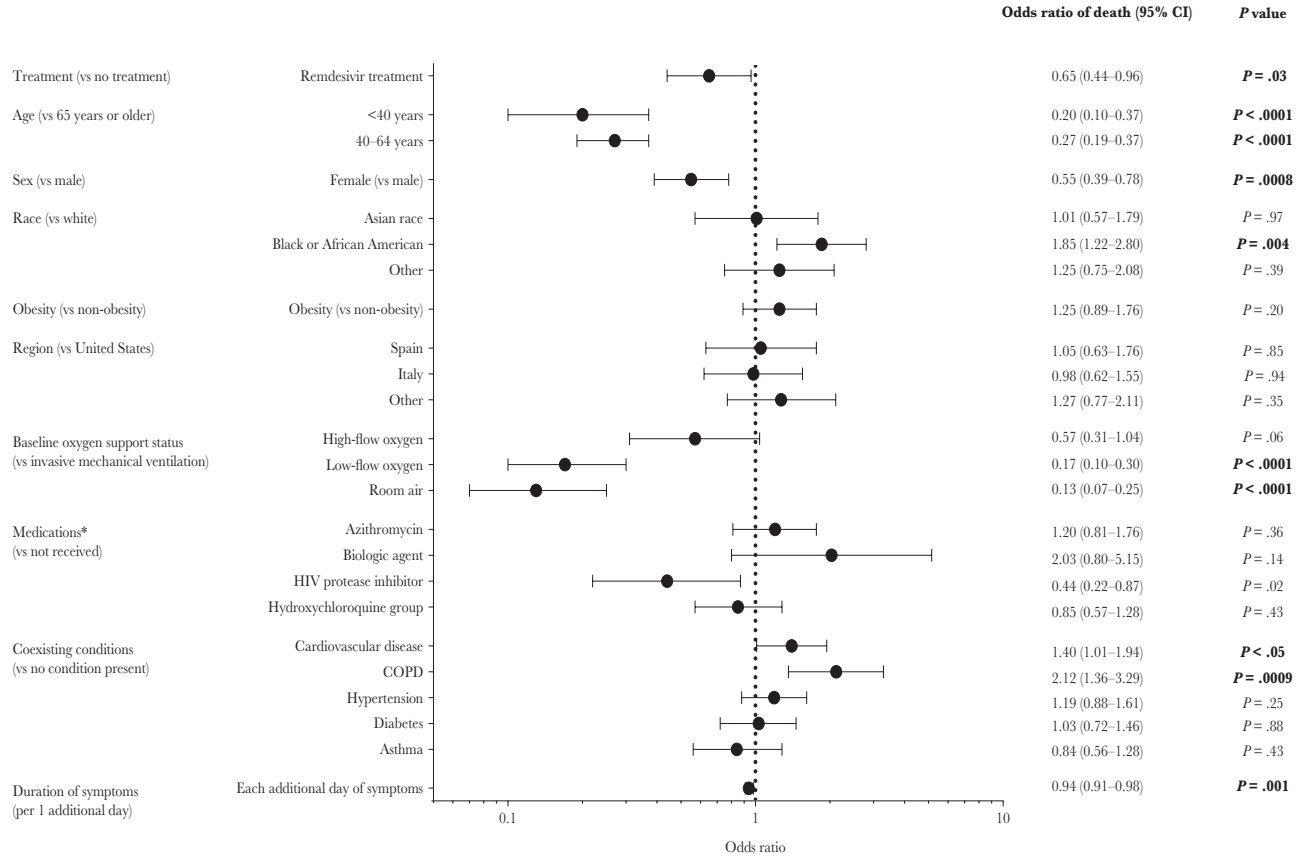

Figure 3. Multivariable analysis of the odds ratio for day 28 all-cause mortality using generalized estimating equation logistic regression model. *Medications potentially active against coronavirus disease 2019. CI, confidence interval; COPD, chronic obstructive pulmonary disease.

mortality benefit of remdesivir for patients on low-flow oxygen at baseline, but no significant effect for patients who required high-flow oxygen or mechanical ventilation at baseline. The subgroup analysis suggests that initiating remdesivir early in the disease course (eg, for patients on low-flow oxygen) may provide the maximum benefit. Limited sample size precluded definitive analyses in other subgroups.

The Solidarity Therapeutics Trial, comparing remdesivir with local standard-of-care, also evaluated mortality and reported a log-rank death rate ratio of 0.95 (95% CI, 0.81–1.11; $P = .50$; 301 of 2743 remdesivir vs 303 of 2708 control) [17]. Baseline oxygen status, other than mechanical ventilation, was not described in the Solidarity study. The subgroup of patients not on mechanical ventilation showed a rate ratio for death of 0.86 (99% CI, 0.67–1.11), which was not significant but used an extremely conservative 99% CI. Commentators have suggested that Solidarity's failure to detect a benefit with remdesivir may be due to variations across trial sites in standards of care, timing of treatment initiation, intensive care unit standards, and disease burden [18, 19].

The efficacy of remdesivir has also been evaluated for moderate COVID-19 [20]. Compared with standard care, patients receiving a 5-day course of remdesivir had a significantly higher odds of a better clinical status distribution on day 11 (OR, 1.65; 95% CI, 1.09–2.48; $P = .02$), whereas the clinical status distribution between the 10-day remdesivir and standard care groups was not significant ($P = .18$) [20], likely due to an interaction by open-label assignment resulting in a bimodal, rather than normal, distribution of date of hospital discharge. Real-world evidence supportive of remdesivir is also starting to accumulate, indicating that remdesivir could potentially have positive effects on clinical improvement and a favorable benefit/risk profile in different patient populations [9, 21, 22].

In light of the growing evidence base around pharmacological interventions, remdesivir is recommended for COVID-19 by the American Thoracic Society/European Respiratory Society Coordinated International Task Force [23], the National Institutes of Health [24], and the Infectious Diseases Society of America [25], as well as in several other national guidelines [3, 26–32]. However, the World Health Organization currently has a conditional recommendation against administering remdesivir in addition to usual care [33]. Further studies are required to identify the optimal combinations of pharmacological agents for treatment regimens including remdesivir.

The multivariable analyses in this study were built upon the growing body of evidence on the factors influencing the

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survival of patients with severe COVID-19, with our model primarily aiming to investigate the robustness of the results of our primary analysis (ie, the treatment effect of remdesivir on mortality). The multivariable OR for treatment effect was comparable with the primary analysis, thereby confirming the treatment effect. In addition, the data suggested that after accounting for treatment arm, a lower risk of mortality was associated with the following: younger age, being female, being white (vs black/African American), being on low-flow oxygen or room air at baseline, receiving an HIV protease inhibitor before or at baseline, not having cardiovascular disease or chronic obstructive pulmonary disease, and (paradoxically) longer duration of symptoms before baseline. These results may differ from previous data in other publications [34–36] due to the nature of the cohorts and the analysis methods (including that our analysis was propensity matched). As noted, however, the model confirmed that remdesivir reduces mortality after accounting for all factors in the model (including duration of symptoms, ethnicity, and other medications).

Strengths and limitations of the present analysis are as previously described [13]. In brief, strengths include the following: the remdesivir data are derived from a large, phase 3 study and detailed patient-level data were available for the nonremdesivir cohort; propensity score matching maximized comparability across treatment groups; and both studies ran in parallel, ensuring consistent standard of care in both populations in the early days of the pandemic. In addition, the 28-day time point is reflective of the protracted course of the disease. Limitations include (1) the comparison of data from a prospective randomized study versus those from a retrospective, observational, nonrandomized treatment cohort, (2) that open-label treatment with remdesivir may be a source of bias (indeed, more patients in the nonremdesivir group received other medications with potential activity against COVID-19), (3) potential residual confounding even after application of propensity score matching, and (4) that the use of unproven treatments for COVID-19 with potentially limited benefit (and potential harm) might have been more widespread in the nonremdesivir cohort. Finally, although the benefits of systemic corticosteroid therapy among hospitalized patients with SARS-CoV-2 infection were demonstrated in the RECOVERY trial [14], our study was conducted before those results. Thus, we did not capture corticosteroid use in the nonremdesivir cohort and could not evaluate the combined impact of remdesivir with corticosteroids.

CONCLUSIONS

Remdesivir was associated with significantly higher rates of day 14 clinical recovery and lower day 28 mortality compared with standard-of-care treatment in hospitalized patients with COVID-19. These data support the use of remdesivir to improve clinical recovery and lower mortality from SARS-CoV-2 infection. In addition, by improving clinical recovery, remdesivir may help to reduce the burden on hospitals during surges in SARS-CoV-2 infections.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Data sharing statement

Gilead Sciences makes available anonymized individual patient data upon request or as required by law or regulation with external researchers. Approval of such requests is at Gilead Sciences' discretion and is dependent on the nature of the request, the merit of the research proposed, the availability of the data, and the intended use of the data. Data requests should be sent to datarequest@gilead.com. Data from GS-US-540-5807 can only be provided with each participating institution's prior written consent.

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