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MAJOR ARTICLE

Compassionate Use of Remdesivir in Pregnant Women With Severe Coronavirus Disease 2019

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Background. Remdesivir is efficacious for severe coronavirus disease 2019 (COVID-19) in adults, but data in pregnant women are limited. We describe outcomes in the first 86 pregnant women with severe COVID-19 who were treated with remdesivir.

Methods. The reported data span 21 March to 16 June 2020 for hospitalized pregnant women with polymerase chain reaction–confirmed severe acute respiratory syndrome coronavirus 2 infection and room air oxygen saturation ≤94% whose clinicians requested remdesivir through the compassionate use program. The intended remdesivir treatment course was 10 days (200 mg on day 1, followed by 100 mg for days 2–10, given intravenously).

Results. Nineteen of 86 women delivered before their first dose and were reclassified as immediate "postpartum" (median postpartum day 1 [range, 0–3]). At baseline, 40% of pregnant women (median gestational age, 28 weeks) required invasive ventilation, in contrast to 95% of postpartum women (median gestational age at delivery 30 weeks). By day 28 of follow-up, the level of oxygen requirement decreased in 96% and 89% of pregnant and postpartum women, respectively. Among pregnant women, 93% of those on mechanical ventilation were extubated, 93% recovered, and 90% were discharged. Among postpartum women, 89% were extubated, 89% recovered, and 84% were discharged. Remdesivir was well tolerated, with a low incidence of serious adverse events (AEs) (16%). Most AEs were related to pregnancy and underlying disease; most laboratory abnormalities were grade 1 or 2. There was 1 maternal death attributed to underlying disease and no neonatal deaths.

Conclusions. Among 86 pregnant and postpartum women with severe COVID-19 who received compassionate-use remdesivir, recovery rates were high, with a low rate of serious AEs.

Keywords. remdesivir; pregnant; COVID-19; ventilation; recovery.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, presents from asymptomatic disease to hypoxemic respiratory failure and death. More than 38 million cases and more than one million deaths have been reported to the World Health Organization as of 14 October 2020 [1]. Remdesivir (GS-5734) is a nucleotide analogue that reduces SARS-CoV-2 replication in vitro through selective inhibition of viral RNA-dependent, RNA polymerase, which SARS-CoV-2 utilizes for replication within host cells [2, 3]. In rhesus macaques infected with SARS-CoV-2, therapeutic remdesivir reduces clinical disease and lung damage [4]. In the Adaptive COVID-19 Treatment Trial (ACTT-1) in nonpregnant hospitalized adults with severe COVID-19, remdesivir for 10 days was superior to placebo in reducing time to recovery, and a randomized, open-label, phase 3 trial (GS-US-540-5773) showed that 5 days of remdesivir resulted in similar outcomes compared with 10 days [5, 6]. Based on these data, emergency use authorization (EUA) was granted by the United States (US) Food and Drug Administration for treatment of adults and children with severe COVID-19 disease [7].

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Women of reproductive age have comprised 21% of all SARS-CoV-2 cases reported to the US Centers for Disease Control and Prevention (CDC) from 22 January to 7 June 2020, 9% of whom were pregnant [8]. Like nonpregnant adults, pregnant women with confirmed SARS-CoV-2 infection develop severe or critical illness in 9%–14% of cases [9, 10]. However, compared to age-matched nonpregnant women with COVID-19, pregnant women are more likely to be hospitalized, admitted to the intensive care unit (ICU), and require invasive mechanical ventilation (IMV) [8]. In a cohort of 64 pregnant women hospitalized with severe or critical COVID-19 at 12 US institutions, adverse pregnancy outcomes were also common, with high rates of preterm birth and cesarean delivery, and most deliveries necessitated due to maternal disease status [11].

There are limited data regarding treatment of COVID-19 in pregnant women, and most come from small case series and case reports [12–14]. Pregnant women have been excluded from clinical trials evaluating remdesivir for COVID-19. However, since 21 March 2020, clinicians were able to request remdesivir for use in pregnant women with severe COVID-19, through a compassionate-use program. Remdesivir is now available for pregnant women with severe COVID-19 through the EUA as of 1 May 2020. In this report, we describe outcomes in the first 86 pregnant women hospitalized for severe COVID-19 who were treated with compassionate-use remdesivir.

METHODS

Compassionate-use Program Description and Population

Gilead Sciences began accepting requests from clinicians for compassionate use of remdesivir in pregnant women with COVID-19 on 21 March 2020 via a single-patient protocol (available at https://academic.oup.com/cid). For each patient treated with remdesivir under compassionate use, regulatory and institutional review board or independent ethics committee approval was obtained, with consent secured for all patients based on local regulations. Access through compassionate use was limited to hospitalized patients with severe COVID-19, defined as presence of SARS-CoV-2 infection, confirmed by reverse-transcription polymerase chain reaction assay, and either oxygen saturation of ≤94% while breathing ambient air or need for oxygen support [5, 6, 15]. Exclusion criteria included creatinine clearance (by Cockcroft-Gault) of <30 mL/minute, serum levels of alanine aminotransferase (ALT) >5 times the upper limit of normal, or evidence of multiorgan failure. Remdesivir is not administered in persons with severe renal impairment due to concern of clearance of cyclodextrin in the intravenous formulation; remdesivir is not associated with renal toxicity. Clinicians were asked not to administer other investigational agents concurrently with remdesivir. The intended remdesivir treatment course was 10 days and comprised a loading dose of 200 mg intravenously (day 1), plus 100 mg intravenously (days 2–10). Supportive therapy and study drug discontinuation were at clinicians' discretion. There was no predetermined number of patients or sites or duration for the program. We report the first 86 women who were pregnant at the time of approval of remdesivir through compassionate use on or before 22 April 2020; they were followed through discharge or death or through 28 days postinitiation. Of these 86 women, 19 women had already delivered by the time they received remdesivir and are referred to herein as the immediate "postpartum" group (median, postpartum day 1 [range, 0–3]). Data for some patients included in this analysis have been reported previously [12–14].

Procedures

This program had no prespecified endpoints. An electronic case report form was used by clinicians to report clinical status, remdesivir administration, adverse events (AEs), selected laboratory results, and pregnancy outcomes, when applicable. No further follow-up under the protocol was required after hospital discharge.

Outcomes

The main clinical outcome was recovery: (1) For women on room air at baseline (ie, entry into the compassionate-use program), recovery was defined as discharge; or (2) for women who were hypoxic and on oxygen support of any kind at baseline, recovery was defined as improving to room air or discharge. For patients on IMV at baseline, we report extubation and time to extubation. Changes in oxygen status are reported using the modified ordinal scale (Supplementary Figure 1) [6, 9, 16], which includes the following categories: (6) death; (5) hospitalized, requiring IMV and/or ECMO; (4) hospitalized, requiring high-flow oxygen therapy and/or noninvasive positive pressure ventilation; (3) hospitalized, requiring supplemental low-flow oxygen therapy; (2) hospitalized on room air; (1) not hospitalized (discharge). We report 2-point improvement or any (1-point) improvement in the ordinal scale. Pregnancy outcomes (reported by treating clinicians) included gestational age at delivery, cesarean delivery, and emergent cesarean delivery. Safety was assessed by AEs and treatment-emergent laboratory abnormalities.

Statistical Methods

Our population included all women who were pregnant at the time of approval for compassionate use of remdesivir on or before 22 April 2020, who had known delivery status on day 1 of dosing, and for whom clinical data for baseline and at least 1 subsequent day were available. Baseline demographic, clinical, and pregnancy characteristics were obtained and stratified by whether participants were pregnant or postpartum prior to remdesivir initiation. No sample size calculation was performed.

We report proportions of patients achieving key clinical outcomes by day 28 and used a competing risk analysis approach, with death as the competing risk, to evaluate time to clinical recovery and time to extubation. Cox proportional hazards regression was used to assess associations between pretreatment characteristics and reported outcomes. We examined associations of the following demographic and clinical characteristics with risk of recovery: (1) baseline invasive ventilation; (2) age (<35 vs ≥35 years); (3) duration of symptoms (<9 vs ≥9 days); and (4) gestational age (<24, 24–32, or >32 weeks). Results are reported as hazard ratio (HR) point estimates and 95% confidence intervals (CIs). The same approach was used for risk of extubation among patients with baseline invasive ventilation.

Pregnancy outcomes were stratified by presence of at least 1 risk factor for high-risk pregnancy. Those included (1) preeclampsia, chronic hypertension, diabetes (gestational or pregestational), chronic kidney disease, systemic lupus erythematosus, and/or obesity; (2) multifetal gestation; or (3) age ≥35 years.

Adverse events and treatment-emergent laboratory abnormalities are summarized. The Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Event, version 2.1 (July 2017) was used for assigning toxicity grades (0 to 4) to laboratory results [17]. All analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Baseline Demographics and Clinical Characteristics

From 21 March 2020, 86 pregnant women were approved for participation in the remdesivir compassionate-use program. Sixty-seven initiated remdesivir while pregnant and 19 initiated it immediately postpartum (median postpartum day 1 [range, 0–3]). The median maternal age was 33 years (range, 20–43 years), and 41% were 35 years or older; there was no difference in median age in pregnant women compared with postpartum women (Table 1). Ninety-one percent of women were treated in the US (Supplementary Table 2). At remdesivir initiation, all women in the postpartum group were in the ICU compared to 67% of pregnant women; all but 1 of the postpartum women required IMV, compared with 40% of pregnant women. One postpartum woman required venovenous ECMO. Median duration of symptoms prior to hospitalization was 9 days, and median duration of hospitalization prior to initiation of remdesivir was 3 days, in both groups. In pregnant women, the most common comorbid medical conditions were obesity (16%), asthma (13%), gestational diabetes (10%), and chronic hypertension (9%); among postpartum women: obesity (21%), gestational diabetes (11%), and chronic hypertension (5%). The median number of remdesivir doses was 8 (interquartile range [IQR], 5–10) for pregnant women, and 10 (IQR, 9–10) for postpartum women. Although clinicians were asked not to administer other investigational agents concurrently with remdesivir, 37% of pregnant women also received hydroxychloroquine and 34% received azithromycin; 37% of postpartum women received hydroxychloroquine and 11% received azithromycin. One person in each group received tocilizumab and 1 pregnant woman received lopinavir/ritonavir.

Clinical Outcomes

The proportion of patients who experienced recovery within 28 days was high among both pregnant and postpartum women. Ninety-three percent of pregnant women and 89% of postpartum women have recovered (Supplementary Figure 1). The highest rates of clinical improvement were among pregnant women not requiring invasive ventilation, of whom 98% recovered, 95% were discharged, 98% had any clinical improvement, and 95% had a 2-point improvement. Of women requiring IMV at baseline, rates of clinical improvement within 28 days were similar in pregnant and postpartum women: survival to discharge, 82% and 83%; any improvement, 93% and 89%; and ≥2-point improvement, 89% and 89%, respectively.

Among pregnant women, 93% recovered and 90% were discharged, with 96% exhibiting any clinical improvement (1 point on ordinal scale, Figure 1A), and 93% experiencing a 2-point improvement on the ordinal scale. Among postpartum women, 90% recovered and 84% were discharged, with 89% exhibiting any clinical improvement (Figure 1B) and 90% exhibiting a 2-point improvement. Among pregnant women, median time to recovery was 5 days for those not on IMV and 13 days for those on IMV ($P < .001$; Figure 2A). Both pregnant and postpartum women on invasive ventilation had median time to recovery of 13 days ($P = .53$; Figure 2A). Pregnant and postpartum women invasively ventilated at baseline had similar times to extubation (11 vs 7 days, $P = .61$; Figure 2B). In the multivariate analysis, for pregnant women, those on IMV at baseline had significantly longer time to recovery (HR, 0.34 [95% CI, .20–.59]; $P = .0001$). For postpartum women, those <35 years of age had a significantly shorter time to recovery (HR, 5.70 [95% CI, 1.01–32.06]; $P = .0482$). No baseline demographic or clinical disease characteristics examined, including duration of symptoms, were significantly associated with time to extubation.

Pregnancy Outcomes

We observed 45 total deliveries, including 26 among women who were pregnant at the time of remdesivir initiation and 19 among women who delivered prior to remdesivir initiation (postpartum group). Of all deliveries, 82% were cesarean and 86% of those were emergent cesarean (Supplementary Figure *3A*). Postpartum women had a numerically higher rate of cesarean delivery (95%) compared with women who initiated remdesivir while pregnant (73%). Of the 26 deliveries among pregnant women, 19 (73%) were cesarean and of these, 17 (89%) were emergent; 18 of the 26 (69%) neonates were delivered very

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Pregnant (n = 67)	Postpartum (n = 19)	All (N = 86)
Age, y, median (range)	33 (21–43)	34 (20–41)	33 (20–43)
Age <35 y	40 (60)	11 (58)	51 (59)
Gestational age, wk, median (range)	28 (14–39)	30 (27–36)	29 (14–39)
Gestational age category, wk			
<24	12 (18)	0	12 (14)
24–32	44 (66)	13 (72)	57 (67)
>32	11 (16)	5 (28)	16 (19)
Duration of hospitalization, d, median (IQR)	3 (2–5)	3 (2–6)	3 (2–5)
Oxygen support category			
Invasive	27 (40)	18 (95)	45 (52)
IMV	27 (40)	17 (90)	44 (51)
ECMO	0	1 (5)	1 (1)
Noninvasive	40 (60)	1 (5)	41 (48)
NIPPV	2 (3)	0	2 (2)
High-flow oxygen	10 (15)	1 (5)	11 (13)
Low-flow oxygen	25 (37)	0	25 (29)
Room air	3 (4)	0	3 (3)
ICU setting	44 (67)	19 (100)	63 (74)
Duration of symptoms before remdesivir, d, median (IQR)	9 (7–11)	9 (6–11)	9 (7–11)
Any medical condition history	45 (67)	10 (53)	55 (64)
Comorbid conditions associated with increased pregnancy/COVID-19 risk			
Obesity[a]	11 (16)	4 (21)	15 (17)
Asthma	9 (13)	1 (5)	10 (12)
Gestational diabetes	7 (10)	2 (11)	9 (10)
Chronic hypertension	6 (9)	1 (5)	7 (8)
Diabetes mellitus[b]	7 (10)	0	7 (8)
Preeclampsia	0	0	0
Median laboratory values, median (IQR)			
ALT, IU/L[c]	24 (15–36)	34 (18–43)	26 (15–39)
AST, IU/L[c]	30 (24–48)	42 (31–67)	32 (25–56)

Data are presented as no. (%) unless otherwise indicated.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IMV, invasive mechanical ventilation; IQR, interquartile range; NIPPV, noninvasive positive-pressure ventilation.

[a]Includes abnormal body mass index (>35 kg/m^2) and obesity.

[b]Includes 2 patients with glucose intolerance.

[c]At baseline, ALT values ranged from 6 to 300 U/L and AST values ranged from 12 to 967 U/L.

preterm at 24–32 weeks' gestation. Among the 19 postpartum women, 18 (95%) had a cesarean delivery, and of those, 15 were emergent (83%). Twelve of the 19 (63%) neonates were delivered very preterm at 24–32 weeks' gestation. No obstetric indications for preterm delivery (eg, spontaneous preterm labor, placental abruption, or preeclampsia) were reported.

Among women who delivered during their hospitalization for COVID-19, most had a high-risk pregnancy due to underlying medical conditions: 69% of pregnant women were considered high risk, compared with 53% of postpartum women (Supplementary Figure 3*B*). Rates of emergent cesarean delivery were similar in pregnant (86%) and postpartum women (80%) with a high-risk pregnancy.

Among the 45 deliveries, there were no neonatal deaths during the observation period. There was 1 spontaneous miscarriage at 17 weeks' gestation in a 32-year-old woman with a history of intravenous drug use, who was admitted with COVID-19 and found to have concurrent *Staphylococcus aureus* bacteremia, tricuspid valve endocarditis, and septic arthritis.

Safety

In the overall cohort, 29% of women experienced an AE and 16% had a serious AE (Table 2). Among pregnant women, AEs occurring in at least 3% of women included anemia, constipation, deep venous thrombosis, dysphagia, unspecified hypertension, hypoxia, nausea, and pleural effusion, reflecting signs and symptoms of pregnancy as well as COVID-19. Seven pregnant women discontinued study drug due to AEs, including 5 due to elevations in liver enzymes concentration, 1 due to nausea, and another due to hemoptysis. No postpartum women had any AEs that led to discontinuation of remdesivir. One 30-year-old woman, who received remdesivir after delivery, died in the postpartum period due to severe acute respiratory distress syndrome and associated cytokine storm; this death was attributed by the treating clinician to underlying COVID-19 and not to remdesivir.

A Pregnant

No. (%)* Posttreatment O_2 Support Status	BL O_2 Support Status: 5 (ECMO/IMV) n = 27†	4 (NIPPV/high-flow O_2) n = 12	3 (low-flow O_2) n = 25	2 (room air) n = 3
6 (death)	0	0	0	0
5 (ECMO/IMV)	2 (7)	0	0	0
4 (NIPPV/high-flow O_2)	1 (4)	1 (8)	0	0
3 (low-flow O_2)	1 (4)	0	0	0
2 (room air)	1 (4)	0	1 (4)	0
1 (discharge)	22 (81)	11 (92)	24 (96)	3 (100)
Any improvement (≥1 point)	93% (25/27)	92% (11/12)	100% (25/25)	100% (3/3)

Worsened
No change
1-point improvement
≥2-point improvement

B Postpartum

No. (%)* Posttreatment O_2 Support Status	BL O_2 Support Status: 5 (ECMO/IMV) n = 18†	4 (NIPPV/high-flow O_2) n = 1	3 (low-flow O_2) n = 0	2 (room air) n = 0
6 (death)	1 (6)	0	0	0
5 (ECMO/IMV)	1 (6)	0	0	0
4 (NIPPV/high-flow O_2)	0	0	0	0
3 (low-flow O_2)	0	0	0	0
2 (room air)	1 (6)	0	0	0
1 (discharge)	15 (83)	1 (100)	0	0
Any improvement (≥1 point)	89% (16/18)	100% (1/1)	0	0

Worsened
No change
1-point improvement
≥2-point improvement

Figure 1. Clinical outcomes in pregnant (*A*) and postpartum (*B*) women treated with remdesivir at day 28. Mechanical ventilation includes invasive ventilation by endotracheal tube or tracheostomy. Blue shading indicates improvement from baseline oxygen support. *%s calculated from BL O2 support groups; †IMV includes invasive ventilation by endotracheal tube or tracheostomy. Abbreviations: BL, baseline; ECMO, extracorporeal membrane oxygenation; IMV, invasive mechanical ventilation; NIPPV, noninvasive positive pressure ventilation; O_2, oxygen.

In this compassionate-use program, data were collected on a limited number of laboratory measures. Sixty-seven percent of all pregnant and postpartum women experienced any treatment-emergent graded laboratory abnormality; most were grade 1 or 2 (Table 2). Grade 3 elevations (>5 timesthe upper limit of normal [ULN]) in ALT and aspartate aminotransferase (AST) occurred in 9% and 5% of pregnant women, and 6% and 6% of postpartum women, respectively. There were no grade 4 elevations (>10 times ULN) of ALT or AST in any women. Most creatinine elevations were grade 1 or 2. Grade 3 elevations in serum creatinine (>1.8 times ULN) occurred in 2% and 11% of pregnant and postpartum women, respectively; grade 4 elevations (>3.5 times ULN) occurred in 5% of pregnant women and no postpartum women.

DISCUSSION

We report experience of the first 86 pregnant women with severe COVID-19 treated in the remdesivir compassionate-use program with 28 days of follow-up. While many women were critically ill at baseline, with 74% admitted to the ICU and 51% receiving IMV, recovery rates were high and treatment with remdesivir was safe and well tolerated.

Clinical recovery from severe COVID-19 was similarly high in women who initiated remdesivir during pregnancy (93%) or the immediate postpartum period (median postpartum day 1 [range, 0–3]) (89%). However, pregnant women not requiring IMV at baseline had the highest rates of recovery (98%) and shortest median time to recovery (5 days). Postpartum women who delivered before initiating remdesivir had more critical illness at baseline, with 100% in the ICU and 95% requiring IMV. Due to the severity of their illness, these women were urgently delivered prior to initiation of remdesivir. When evaluating only those women receiving invasive ventilation at baseline, pregnant and postpartum women had the same median time to recovery (13 days).

In this cohort of women with severe COVID-19, deliveries were often very preterm (67% at <32 weeks' gestational age) and by cesarean (82%); most cesarean deliveries were emergent (86%). Preterm deliveries were likely driven by the severity of maternal COVID-19 illness, as no obstetric indications

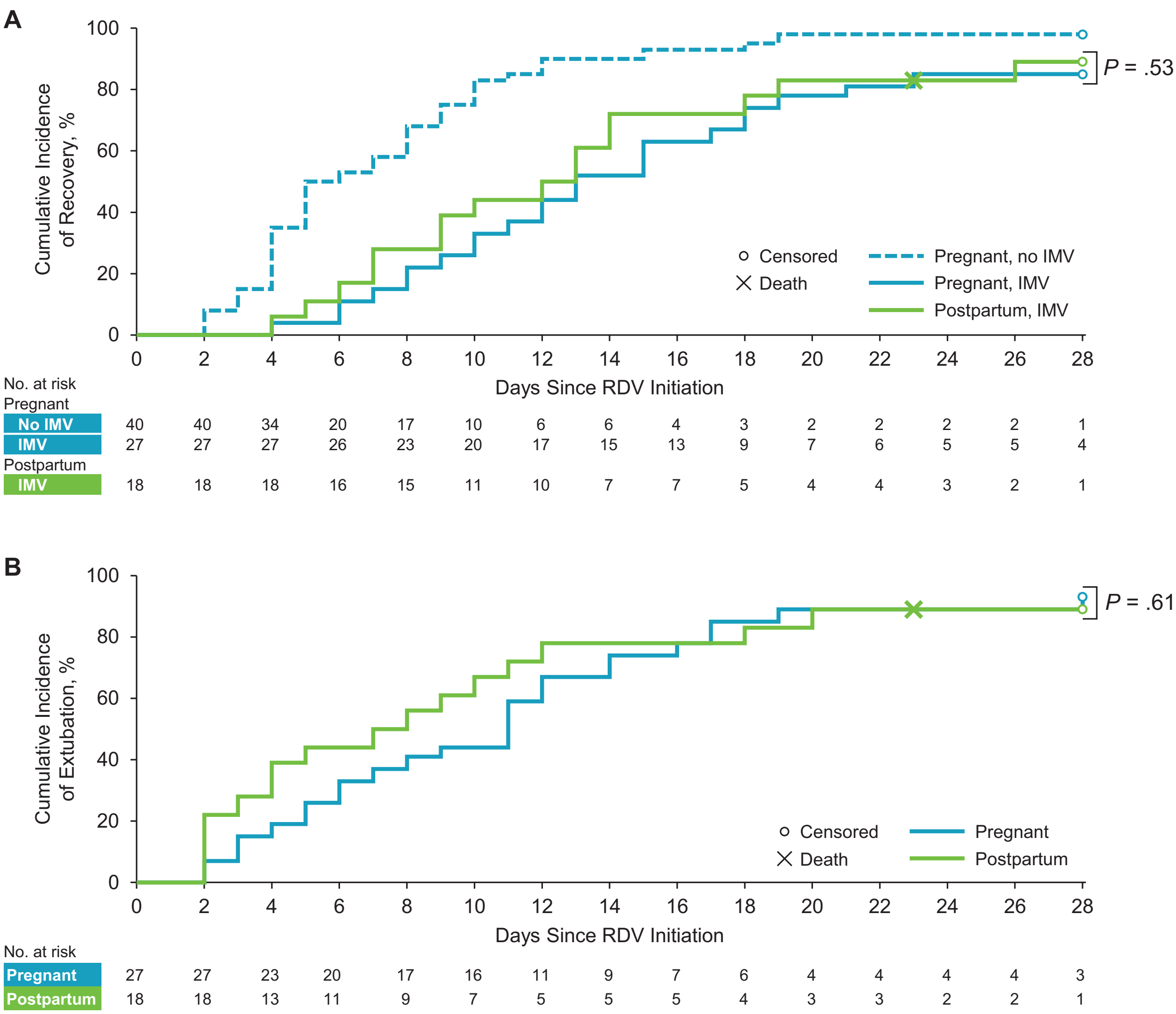

Figure 2. Time to recovery and extubation in pregnant women who received remdesivir. *A*, Time to recovery by baseline oxygen support status (invasive vs not invasive). *B*, Time to extubation: baseline invasive oxygen support. Abbreviations: IMV, invasive mechanical ventilation; RDV, remdesivir.

for delivery were reported by clinicians, including no reports of spontaneous preterm labor, placental abruption, or preeclampsia. Mechanical ventilation alone is not an indication for delivery, and in women <32 weeks' gestation with severe hypoxemia, obstetric societies now recommend consideration of all other options before delivery, including prone positioning, ECMO, and other advanced ventilator methods [18]. Thus, the high number of preterm deliveries is consistent with national data, where a 75% rate of preterm birth was reported in pregnant women with critical COVID-19 [11].

Despite a high number of women with critical COVID-19 in our population, remdesivir was well tolerated. A low number of serious AEs was observed and few led to discontinuation of therapy. No new safety signals were detected in this compassionate-use cohort. The most common AEs were related to pregnancy and underlying disease and most laboratory abnormalities were grade 1 or 2. Grade 3 ALT or AST abnormalities were infrequent; no grade 4 abnormalities were reported. Transient mild to moderate aminotransferase elevations have been observed following remdesivir exposure in healthy volunteers and patients infected with Ebola virus [19]. However, elevated aminotransferase levels are commonly seen in patients with severe COVID-19 prior to treatment [20, 21]. There was 1 maternal death due to underlying disease and no neonatal deaths.

Interpretation of these data is limited as this was not a clinical trial but rather a compassionate-use program with small sample size, lack of placebo comparator arm, and incomplete obstetric and neonatal outcome data. In particular, as postpartum women who participated in this program had more severe COVID-19 disease during their pregnancy, our data may not be generalizable to women diagnosed

Table 2. Overall Safety Summary

Adverse Events	Pregnant Women (n = 67)	Postpartum Women (n = 19)	All Women (N = 86)
Any AE	22 (33)	3 (16)	25 (29)
Any AE in >1% overall			
Anemia	2 (3)	0	2 (2)
Constipation	2 (3)	0	2 (2)
Deep vein thrombosis	2 (3)	0	2 (2)
Dysphagia	2 (3)	0	2 (2)
Unspecified hypertension	2 (3)	0	2 (2)
Hypoxia	2 (3)	0	2 (2)
Nausea	2 (3)	0	2 (2)
Pleural effusion	2 (3)	0	2 (2)
ARDS	1 (1)	1 (5)	2 (2)
Any serious AE	12 (18)	2 (11)	14 (16)
Any AE leading to discontinuation	7 (10)	0	7 (8)
Death	0	1 (5)	1 (1)
Any grade laboratory abnormality	42/67 (64)	14/18 (78)	56/84 (67)
Any grade 3 or 4 laboratory abnormality	12/67 (18)	3/18 (17)	15/84 (18)
Relevant TE laboratory abnormalities[a]			
ALT			
No.	64	17	81
Grade 1	10 (16)	3 (18)	13 (16)
Grade 2	8 (13)	1 (6)	9 (11)
Grade 3	6 (9)	1 (6)	7 (9)
Grade 4	0	0	0
AST			
No.	62	17	79
Grade 1	10 (16)	6 (35)	16 (20)
Grade 2	12 (19)	2 (12)	14 (18)
Grade 3	3 (5)	1 (6)	4 (5)
Grade 4	0	0	0
Creatinine			
No.	65	18	83
Grade 1	2 (3)	2 (11)	4 (5)
Grade 2	5 (8)	2 (11)	7 (8)
Grade 3	1 (2)	2 (11)	3 (4)
Grade 4	3 (5)	0	3 (4)

Data are presented as no. (%).

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; ARDS, acute respiratory distress syndrome; AST, aspartate aminotransferase; TE, treatment-emergent.

[a]Defined as results that increase at least 1 toxicity grade from baseline at any postbaseline time point. If the relevant baseline laboratory result is missing, any abnormality of at least grade 1 observed postbaseline is considered treatment-emergent.

in the postpartum period with milder disease. Moreover, safety and efficacy of remdesivir in women diagnosed in the postpartum period may be gleaned from adult randomized controlled trials [5, 6]. Further investigation using a larger sample size and longer follow-up time is needed to determine the potentially variable effects of disease severity, pregnancy status, and delivery status on clinical outcomes. Furthermore, voluntary data entry into the online system occurred amidst challenges of clinical practice during the pandemic, and as such medical history, clinical course details, and AE reporting may not have been as systematically reported as in conventional clinical trials. Unlike dedicated laboratory tests conducted centrally for clinical trials, laboratory values from diverse clinical care settings and their local laboratories were individually entered, so data are only available on a limited number of relevant laboratory values. Data on viral shedding were not available universally and not collected for women or for delivered infants. We did not collect race or ethnicity data. Last, we would like to note that management of the disease has changed over time and continues to evolve with emerging data. The 86 women in our cohort were hospitalized and treated with remdesivir in the early days of the pandemic. Initially, some obstetric providers delivered patients early due to limited knowledge about the disease and concern for maternal/fetal decompensation. Our data also reflect a longer time from symptom onset to remdesivir initiation, which will likely decrease with evolving clinical practice.

Despite these limitations, these data from the first 86 pregnant women treated with remdesivir under compassionate use suggest that remdesivir was safe and well tolerated. Moreover, women in this analysis had higher rates of recovery than nonpregnant adults in the adult compassionate-use program (92% vs 62%) [22], although the 2 populations were different; for example, pregnant women were considerably younger (median age 33 vs 64 years). Finally, our results with remdesivir were achieved despite a high number of critically ill pregnant women, whereas among hospitalized pregnant women reported to the US CDC with SARS-CoV-2 infection, only 4.6% had known ICU admission [8].

Given recent data that pregnant women with COVID-19 are more likely to be admitted to the ICU and require invasive ventilation compared with nonpregnant women of reproductive age, the present analysis suggesting at least similar clinical and safety outcomes for remdesivir use in pregnant women provides a strong rationale to include pregnant women in remdesivir clinical trials and access programs, as has been strongly advocated for by those who care for pregnant women [23–25].

In summary, results from the compassionate-use program provide strong support that remdesivir is safe in pregnant women with high rates of clinical recovery. Inclusion of pregnant women in future remdesivir clinical trials is essential to better characterize pharmacokinetics, safety, and efficacy of remdesivir use in pregnancy as well as neonatal outcomes in this understudied population.

Supplementary Data

Supplementary materials are available at *Clinical 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.

Notes

Author contributions. All authors were given access to the reported data and took responsibility for their integrity and completeness. The initial draft of the manuscript was prepared by R. M. B. and M. D.

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