SARS-CoV-2 Viral Load Dynamics in Participants With Solid Organ Transplantation and Severely Reduced Kidney Function From the Remdesivir Phase 3 REDPINE Study Who Were Hospitalized for COVID-19

P-1625
REDPINE

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Conclusions

- In the REDPINE study, remdesivir treatment reduced SARS-CoV-2 viral load compared with placebo
- Among remdesivir-treated participants, baseline viral load was higher and viral load reductions were slower in solid organ transplant recipients who were on immunosuppressive drugs compared with those who were not solid organ transplant recipients, potentially due to diminished immune system support to clear the virus
- A model of viral load in kidney transplant recipients predicted a faster reduction in viral load after 10 days of remdesivir treatment compared with 5 days of treatment
- These findings suggest that extending the duration of remdesivir treatment beyond 5 days may be beneficial in mitigating prolonged viral shedding in solid organ transplant recipients

Plain Language Summary

- People who have had an organ transplant, such as a kidney transplant, typically have to take drugs so that their immune system does not attack the transplanted organ
  - — However, these drugs weaken the immune system, which is the body's natural defense system that helps fight against bacterial and viral infections
- Remdesivir is a drug that stops replication of SARS-CoV-2, the virus that causes COVID-19
- This study found that people who had organ transplants and were treated with remdesivir took longer to clear SARS-CoV-2 from their bodies compared with people who had not had organ transplants and were treated with remdesivir
- These results suggest that people who have had organ transplants may need to take remdesivir longer to help them clear the virus

References: **1.** Rahmani A, et al. *Med Lav*. 2022;113:e2022014. **2.** Raglow Z, et al. *Lancet Microbe*. 2024;5:e235-46. **3.** Christofferson RC, et al. *Influenza Other Respir Viruses*. 2025;19:e70121. **4.** VEKLURY® (remdesivir) for injection, for intravenous use [package insert]. Gilead Sciences, Inc.; 2025. **5.** Sise ME, et al. *Clin Infect Dis*. 2024;79:1172-81. **6.** Andreatta K, et al. *Open Forum Infect Dis*. 2023;10:ofad500.575.

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Introduction

- Prolonged shedding of SARS-CoV-2 has been documented in viral dynamics studies of people with immunocompromising conditions, including solid organ transplant (SOT) recipients[1-3]
- Remdesivir (RDV) is a nucleotide analog prodrug approved for the treatment of COVID-19 in hospitalized and nonhospitalized patients[4]
- The REDPINE study was a Phase 3 randomized controlled trial that demonstrated the safety of RDV for the treatment of COVID-19 in hospitalized participants with severe renal impairment[5]
  - — SARS-CoV-2 resistance analyses of REDPINE found that, of the 4 participants with treatment-emergent substitutions in Nsp12 that conferred low reductions in RDV susceptibility, 3 participants were SOT recipients who received concomitant immunosuppressive medications during the study[6]

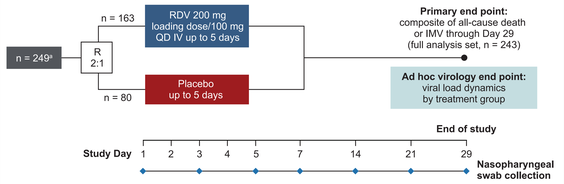
Objective

- To analyze SARS-CoV-2 viral load dynamics in participants from the REDPINE study who were SOT recipients

Methods

- REDPINE was a double-blind, placebo-controlled trial in which participants with severely reduced kidney function who were hospitalized for COVID-19 were randomized 2:1 to receive RDV or placebo for 5 days (**Figure 1**)[5]

Figure 1. REDPINE Study Design[5]



[a]249 participants were randomized, but 6 were not treated.
IMV, invasive mechanical ventilation; IV, intravenous; QD, once daily; R, randomization; RDV, remdesivir.

- Nasopharyngeal swab samples were collected on Days 1 (baseline), 3, 5, 7, 14, 21, and 29 to assess SARS-CoV-2 viral load by means of quantitative reverse transcriptase–polymerase chain reaction (RT-qPCR)
- The virology analysis set included all participants who were randomized into the study, received ≥1 dose of the study drug, and had positive SARS-CoV-2 RT-qPCR at baseline
- The change from baseline in SARS-CoV-2 viral load was compared in an ad hoc analysis using a mixed model for repeated measures (MMRM) approach between (1) the RDV and placebo groups, (2) RDV-treated participants who had (SOT recipients) or had not received an SOT (non–SOT recipients), and (3) RDV-treated participants who received a kidney transplant versus non–SOT recipients
- Two models (on-treatment viral load and posttreatment viral load change) were built to predict the effect of extending RDV treatment duration on viral load dynamics
  - — To account for the hierarchical structure of the data and repeated measures within individuals, a linear mixed-effects model was employed using the lme4 package in R (version 4.3.1)
  - — The on-treatment model for participant i was specified as follows:

$$VL = \beta_0 + T + u_i + \epsilon$$

where VL was the viral load, β_0 was the baseline parameter, T was the fixed-effect time on treatment, u_i was the mixed-effect term for each participant to account for variability within individuals, and ϵ was the noise term

  - — The posttreatment model for participant i was specified as follows:

$$\Delta VL = \beta_0 + \Delta T + u_i + \epsilon$$

where ΔVL was the change in viral load after treatment, β_0 was the baseline parameter, ΔT was the fixed-effect time after treatment, u_i was the mixed-effect term for each participant to account for variability within individuals, and ϵ was the noise term

Results

Participants

- Of the 243 (RDV, 163; placebo, 80) participants who were enrolled and treated in the study, 42 (RDV, 35 [21%]; placebo, 7 [9%]) had a history of SOT and received immunosuppressive drugs prior to and during the study
  - — Of these, 34 (RDV, 28 [80%]; placebo, 6 [86%]) participants had a history of kidney transplantation

Viral Load Dynamics by Study Drug and SOT Status

- Overall, the observed mean SARS-CoV-2 viral load at baseline was similar between the RDV and placebo groups (**Table 1**)

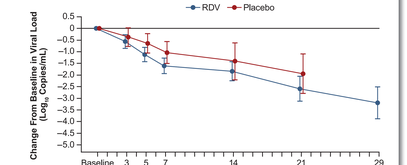
Table 1. SARS-CoV-2 Viral Load (Log_{10} Copies/mL) at Baseline (Virology Analysis Set[a])

	Mean (SD)	Median (Q1, Q3)
RDV (n = 127)	5.9 (1.5)	6.2 (4.9, 7.0)
SOT recipients (n = 29)	6.5 (1.2)	6.4 (6.3, 7.1)
Kidney transplant recipients (n = 23)	6.4 (1.3)	6.4 (6.0, 7.1)
Non–SOT recipients (n = 98)	5.8 (1.5)	5.8 (4.5, 6.9)
Placebo (n = 54)	6.2 (1.5)	6.1 (5.0, 7.5)

[a]Virology analysis set included all participants who were randomized into the study, received ≥1 dose of the study drug, and had positive SARS-CoV-2 RT-qPCR at baseline.
Q1, first quartile; Q3, third quartile; RDV, remdesivir; RT-qPCR, quantitative reverse transcriptase–polymerase chain reaction; SOT, solid organ transplant.

- MMRM analyses demonstrated that RDV treatment led to significantly greater reductions from baseline in viral load on Day 5 (least squares mean [LSM] difference, −0.48 log_{10} copies/mL; $P = 0.033$) and Day 7 (−0.57 log_{10} copies/mL; $P = 0.034$) compared with placebo (**Figure 2**)

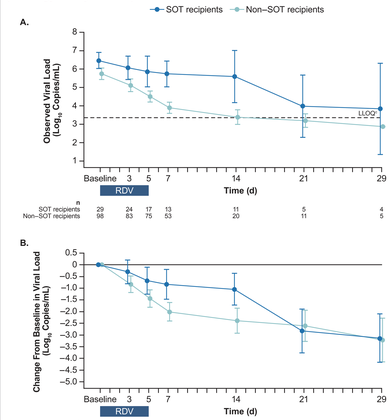
Figure 2. LSM (95% CI) Change From Baseline[a] in SARS-CoV-2 Viral Load by Study Drug (Virology Analysis Set[b])



[a]LSM change from baseline in viral load and *P* values were determined using MMRM.
[b]Virology analysis set included all participants who were randomized into the study, received ≥1 dose of the study drug, and had positive SARS-CoV-2 RT-qPCR at baseline.
LSM, least squares mean; MMRM, mixed model for repeated measures; RDV, remdesivir; RT-qPCR, quantitative reverse transcriptase–polymerase chain reaction.

- Among RDV-treated participants, the observed mean SARS-CoV-2 viral load was higher in SOT recipients compared with non–SOT recipients from baseline through Day 29 (**Figure 3A**)
  - — When comparing SOT recipients and non–SOT recipients, 3/11 (27%) versus 14/20 (70%), respectively, reached the lower limit of quantification (LLOQ) for the RT-qPCR viral load assay on Day 14
- RDV-treated SOT recipients had significantly smaller viral load reductions from baseline on Days 5, 7, and 14 compared with RDV-treated non–SOT recipients (all P <0.05; **Figure 3B**)

Figure 3. (A) Observed Mean (SD) and (B) LSM (95% CI) Change From Baseline[a] in SARS-CoV-2 Viral Load by SOT Status (Virology Analysis Set[b])



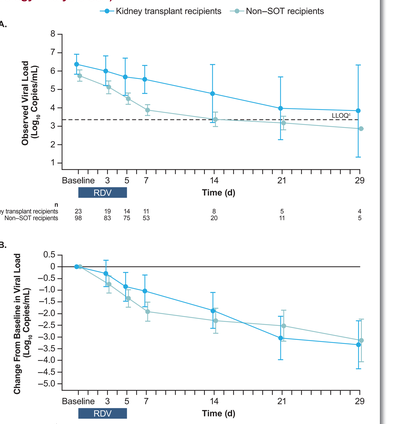
[a]LSM change from baseline in viral load and *P* values were determined using MMRM.
[b]Virology analysis set included all participants who were randomized into the study, received ≥1 dose of the study drug, and had positive SARS-CoV-2 RT-qPCR at baseline.
[c]The LLOQ of the RT-qPCR viral load assay was 3.35 log_{10} copies/mL.
LLOQ, lower limit of quantification; LSM, least squares mean; MMRM, mixed model for repeated measures; RDV, remdesivir; RT-qPCR, quantitative reverse transcriptase–polymerase chain reaction; SOT, solid organ transplant.

- Among RDV-treated participants, the observed mean SARS-CoV-2 viral load was higher in kidney transplant recipients compared with non–SOT recipients from baseline through Day 29 (**Figure 4A**)
  - — When comparing kidney transplant recipients and non–SOT recipients, 3/8 (38%) versus 14/20 (70%), respectively, reached the LLOQ for the RT-qPCR viral load assay on Day 14
- Kidney transplant recipients had smaller reductions from baseline in viral load compared with non–SOT recipients, with a statistically significant difference on Day 7 ($P = 0.025$; **Figure 4B**)

Modeling of Viral Load by RDV Treatment Duration

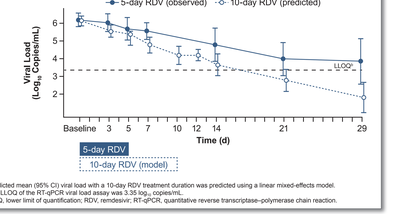
- Viral load dynamics for a 10-day RDV treatment duration were predicted by fitting baseline to Day 5 viral load data from kidney transplant recipients to an on-treatment model and post–Day 5 viral load change data to a posttreatment model (**Figure 5**)
  - — The model predicted that viral load would reach the LLOQ >13 days faster with a 10-day RDV treatment duration (mean viral load <LLOQ at Day 16) versus a 5-day RDV treatment duration (mean viral load >LLOQ at Day 29)

Figure 4. (A) Observed Mean (SD) and (B) LSM (95% CI) Change From Baseline[a] in SARS-CoV-2 Viral Load by Kidney Transplant Status (Virology Analysis Set[b])



[a]LSM change from baseline in viral load and *P* values were determined using MMRM.
[b]Virology analysis set included all participants who were randomized into the study, received ≥1 dose of the study drug, and had positive SARS-CoV-2 RT-qPCR at baseline.
[c]The LLOQ of the RT-qPCR viral load assay was 3.35 log_{10} copies/mL.
LLOQ, lower limit of quantification; LSM, least squares mean; MMRM, mixed model for repeated measures; RDV, remdesivir; RT-qPCR, quantitative reverse transcriptase–polymerase chain reaction; SOT, solid organ transplant.

Figure 5. Predicted Mean (95% CI) SARS-CoV-2 Viral Load Over Time With a 5-Day Versus 10-Day RDV Treatment Duration[a] in Kidney Transplant Recipients



[a]Predicted mean (95% CI) viral load with a 10-day RDV treatment duration was predicted using a linear mixed-effects model.
[b]The LLOQ of the RT-qPCR viral load assay was 3.35 log_{10} copies/mL.
LLOQ, lower limit of quantification; RDV, remdesivir; RT-qPCR, quantitative reverse transcriptase–polymerase chain reaction.