GILEAD | Medical Information

Veklury® (remdesivir) Use in Dialysis

This document is in response to your request for information regarding the use of Veklury® (remdesivir [RDV]) in patients on dialysis. This response was developed according to principles of evidence-based medicine and contains data from prospective and retrospective studies (N≥80).

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.

Summary

Product Labeling[1]

No dosage adjustment of RDV is recommended in patients with any degree of renal impairment, including patients on dialysis. RDV may be administered without regard to the timing of dialysis.

Clinical Data on RDV Use in Patients on Dialysis

In a Japanese cohort study on RDV use in patients with severe renal insufficiency (N=1449), the RDV group had a lower risk of death or IMV/ECMO than the control group (HR, 0.44; 95% CI: 0.23–0.83). In a subgroup analysis of patients who required maintenance dialysis prior to admission, treatment with RDV was associated with a decreased risk of IMV/ECMO compared with control (HR, 0.15; 95% CI: 0.03–0.66).[2]

The REDPINE study evaluated the safety and efficacy of RDV (n=163) compared to placebo (n=80) in participants with severely reduced kidney function (eGFR <30 mL/min/1.73 m^2, including patients with ESRD on chronic dialysis) who were hospitalized for COVID-19. The study stopped enrollment early due to recruitment challenges. The decision was not based on efficacy or safety concerns.[3]

- At baseline, 89 participants (37%) had ESRD on chronic dialysis: 59 participants (36%) in the RDV group and 30 (38%) in the placebo group.[3]
- Among participants with ESRD on chronic dialysis, there was not a significant difference between the RDV and placebo groups in the incidence of the composite endpoint of all-cause death or IMV through Day 29.[3]
- In the overall population, safety outcomes were similar between participants treated with RDV and those treated with placebo. Safety outcomes were not reported based on baseline kidney disease status.[3]

In a retrospective study of 392 Japanese patients who required dialysis, a multivariate analysis of the entire study population revealed that the mortality risk was significantly lower among those treated with RDV than among those who did not receive RDV (P=0.041).[4]

Product Labeling[1]

Dosage and Administration

Renal impairment

No dosage adjustment of RDV is recommended in patients with any degree of renal impairment, including patients on dialysis. RDV may be administered without regard to the timing of dialysis.

Use in Specific Populations

Renal impairment

Use of RDV in patients with COVID-19 and renal impairment, including those on dialysis, is supported by safety and pharmacokinetic data from the following:

- a randomized, double-blind, placebo-controlled trial (Study 5912) in adults;
- an open-label, parallel-group, single-dose trial in participants with normal renal function and renal impairment (Study 9015)

Please refer to the US FDA-approved prescribing information for additional information regarding renal impairment in Sections 2.4 Renal Impairment, 6.1 Clinical Trials Experience, 8.4 Pediatric Use, 8.6 Renal Impairment, and 12.3 Pharmacokinetics.

Clinical Data on RDV Use in Patients on Dialysis

Japanese Cohort Study in Severe Renal Insufficiency[2]

Study design

A retrospective cohort study using data from a nationwide registry of inpatients with COVID-19 in Japan assessed whether RDV initiation within 2 days of admission reduced the risk of mortality or IMV/ECMO in patients with severe renal insufficiency (SCr ≥3 mg/dL, on maintenance dialysis, or kidney transplant recipients). Included in the analysis were 1449 patients with a positive COVID-19 test result who were admitted to a hospital between January 2020 and May 2023 and had preexisting severe renal insufficiency before admission. The primary endpoint was the composite of death and IMV/ECMO, and patients were followed for up to 28 days from Day 7 of COVID-19 symptom onset until discharge, transfer, or death.

Preexisting hemodialysis was reported in 101/272 patients (37.1%) in the RDV group and in 507/1177 patients (43.1%) in the control group.

Results

Death or IMV/ECMO was reported in 19/272 patients (7%) in the RDV group and in 136/1177 patients (11.6%) in the control group, and the RDV group had a lower risk of death or IMV/ECMO than the control group (HR, 0.44; 95% CI: 0.23–0.83). In a subgroup analysis of patients who required maintenance dialysis prior to admission, treatment with RDV was

associated with a decreased risk of IMV/ECMO compared with control (RDV, 5/101 [5%]; control, 56/507 [11.1%]; HR, 0.15; 95% CI: 0.03–0.66).

Safety data were not reported.

REDPINE: RDV and Severely Reduced Kidney Function

Study design

A phase 3, randomized (2:1), double-blind, placebo-controlled, multicenter study evaluated the safety and efficacy of RDV (n=163; 200 mg loading dose via IV infusion on Day 1, followed by 100 mg daily IV infusion up to Day 5) compared to placebo (n=80; IV saline daily[5]) in participants with moderately to severely reduced kidney function (eGFR <30 mL/min/1.73 m^2, including participants with ESRD on chronic dialysis) who were hospitalized for COVID-19 pneumonia. Participants in both arms received standard-of-care. Participants aged ≥12 years were eligible for study enrollment; however, no participants <18 years of age enrolled in the study. Participants who required IMV, NIV, ECMO, or renal replacement therapy for AKI were not eligible for study enrollment. The primary endpoint was a composite of all-cause mortality and the initiation of IMV through Day 29. No renal dose adjustment was required for those assigned to receive RDV. There were 249 participants enrolled in the study; 6 of those participants were not treated.[3]

Of the 243 participants who received treatment, 89 (37%) had ESRD on chronic dialysis: 59 participants (36%) in the RDV group and 30 (38%) in the placebo group.[3]

Efficacy results[3]

In the Kaplan-Meier estimates, there was no significant difference between the RDV and placebo groups in the composite endpoint of all-cause death or IMV through Day 29 (RDV: 30%; placebo: 34%; HR, 0.82; 95% CI: 0.5–1.32; *P*=0.61). This remained true regardless of baseline kidney disease status (ESRD on chronic dialysis: HR, 1.06; 95% CI: 0.48–2.36; *P*=0.88; AKI: HR, 0.84; 95% CI: 0.4–1.77; *P*=0.65; chronic kidney disease: HR, 0.81; 95% CI: 0.3–2.18; *P*=0.67). However, due to insufficient enrollment, the study was not powered to determine a difference between the study arms in efficacy outcomes.

Safety results[3]

Safety data are only available for all participants, including participants with ESRD on chronic dialysis. Overall, 131 participants (80%) in the RDV group and 62 participants (78%) in the placebo group experienced ≥1 TEAE. The most frequently reported TEAEs were hypotension (RDV: n=18 [11%]; placebo: n=4 [5%]), respiratory failure (RDV: n=10 [6%]; placebo: n=10 [13%]), and constipation (RDV: n=12 [7%]; placebo: n=7 [9%]). Serious TEAEs occurred in 82 participants (50%) in the RDV group and 40 participants (50%) in the placebo group; none of these were considered treatment related. Premature study drug discontinuation due to a TEAE occurred in 8 participants (5%) in the RDV group and 1 participant (1%) in the placebo group.

Retrospective Study of Japanese Patients on Dialysis[4]

Study design and demographics

A retrospective study assessed the survival rate and risk factors associated with mortality among Japanese patients hospitalized for COVID-19 who required dialysis. The COVID-19

Task Force Committee in Japan established a registry to follow new cases of COVID-19 in Japanese dialysis facilities on April 8, 2020, and patient data registered by June 19, 2021, were included for this analysis.

In the overall patient population (N=1010), 699 patients (69.2%) recovered, and 311 (30.8%) died. A total of 392 patients were included in the analysis of patients stratified by administration of RDV, which included 98 patients treated with RDV, and were PS-matched to 294 patients who did not receive RDV.

Table 1. Select Baseline Demographics of PS-Matched Patients According to RDV Treatment[4]

Key Demographics and Characteristics		RDV (n=98)	No RDV (n=294)
Age, <60/60–69 /≥70 years, n (%)		30 (30.6)/17 (17.3)/51 (52)	90 (30.6)/51 (17.3)/153 (52)
Male, n (%)		67 (68.4)	210 (71.7)
Primary disease, n (%)	DM/chronic glomerulonephritis/ nephrosclerosis/others	43 (48.3)/20 (22.5)/ 12 (13.5)/14 (15.7)	149 (56.2)/40 (15.1)/ 39 (14.7)/37 (14)
Duration of dialysis, <1/1–4/5–9/10–14/≥15 years, n (%)		14 (14.4)/31 (32)/ 30 (30.9)/13 (13.4)/9 (9.3)	37 (12.9)/100 (34.8)/ 72 (25.1)/42 (14.6)/36 (12.5)
Comorbidities, n (%)	Hypertension	56 (57.1)	127 (44.9)[a]
	DM	52 (53.1)	161 (56.5)
	Cardiovascular disease	46 (48.4)	120 (43.5)
Oxygenation, n (%)	No/yes/ventilator or ECMO	23 (23.5)/53 (54.1)/ 22 (22.4)	69 (23.5)/159 (54.1)/ 66 (22.4)

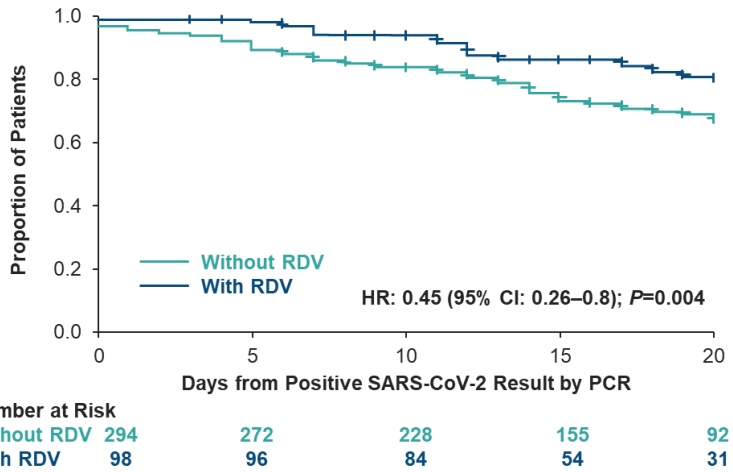
[a]*P*=0.046.

Results

According to multivariate analyses of the entire study population, the mortality risk was significantly lower among those treated with RDV than those who did not receive RDV (HR, 0.6; 95% CI: 0.37–0.98; *P*=0.041).

For the analysis of mortality among those who did and did not receive RDV in the PS-matched cohort, overall survival was significantly greater among those who received RDV than those who did not (Figure). The mean (SD) duration of hospitalization was significantly shorter among those who received RDV than those who did not: 16.2 (8.1) days vs 20.9 (13.2) days, respectively; difference, 4.7 days (95% CI: 2.2–7.4); *P*<0.001.

Figure 1. Overall Survival of PS-Matched Patients According to RDV Treatment[4]



Abbreviation: PCR=polymerase chain reaction.

References

1. Veklury, Gilead Sciences Inc. VEKLURY® (remdesivir) for injection, for intravenous use. U. S. Prescribing Information. Foster City, CA.
2. Yamada G, Ogawa Y, Iwamoto N, et al. Effectiveness of remdesivir in patients with COVID-19 and severe renal insufficiency: a nationwide cohort study in Japan. *Infect Dis (Lond).* 2025;57(2):192-201.
3. Ramon-Santos J, Goldman JD, Tuttle KR, et al. The REDPINE Study: Efficacy and Safety of Remdesivir in People With Moderately and Severely Reduced Kidney Function Hospitalised for COVID-19 Pneumonia [Poster P2635]. Paper presented at: 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID),; April 15-18, 2023; Copenhagen, Denmark.
4. Kikuchi K, Nangaku M, Ryuzaki M, et al. Survival and predictive factors in dialysis patients with COVID-19 in Japan: a nationwide cohort study. *Ren Replace Ther.* 2021;7(1):59. https://www.ncbi.nlm.nih.gov/pubmed/34697570
5. ClinicalTrials.gov. Study to Evaluate the Efficacy and Safety of Remdesivir in Participants With Severely Reduced Kidney Function Who Are Hospitalized for Coronavirus Disease 2019 (COVID-19). ClinicalTrials.gov Identifier: NCT04745351. Available at: https://clinicaltrials.gov/ct2/show/NCT04745351. Accessed: 10 February. Last Updated: 09 February. 2021.

Abbreviations

AKI=acute kidney injury
DM=diabetes mellitus
ECMO=extracorporeal membrane oxygenation
ESRD=end-stage renal disease
HR=hazard ratio
IMV=invasive mechanical ventilation
NIV=non-invasive ventilation
PS=propensity score
RDV=remdesivir
TEAE=treatment-emergent adverse event

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Veklury US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 https://www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.