GILEAD | Medical Information

Veklury® (remdesivir) Use in Severe Renal Impairment

This document is in response to your request for information regarding the use of Veklury® (remdesivir [RDV]) in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2). This response was developed according to principles of evidence-based medicine and contains data from phase 3 clinical trials.

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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 Participants With Severe Renal Impairment

The REDPINE study evaluated the safety and efficacy of RDV (n=163) compared with placebo (n=80) in participants with severely reduced kidney function (eGFR <30 mL/min/1.73 m^2, including participants with kidney failure on chronic dialysis) or AKI 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.[2]

- No significant difference in the incidence of the composite endpoint of all-cause death or IMV through Day 29 was observed between the RDV and placebo groups; however, due to insufficient enrollment, the study was not powered to determine a difference in efficacy outcomes between the study groups.
- Overall rates of AEs were similar in participants treated with RDV and those treated with placebo: 80.4% vs 77.5%, respectively.
- The proportion of participants who developed new or progressive AKI, required RRT, or died were similar in the RDV and placebo groups, regardless of baseline AKI or CKD status.

In a post hoc analysis of 59 hospitalized participants with severe renal impairment (CrCl <30 mL/min/1.73 m^2) who were enrolled in the CATCO study in Canada, there was no increased risk of eGFR decline at Day 5, new dialysis, or mortality among those who received RDV (n=34) compared with those who received SoC (n=25).[3]

Clinical Data on RDV Use in Participants With Severe Renal Impairment

REDPINE: RDV in Severely Reduced Kidney Function or AKI

Study design and demographics[2]

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 Days 2–5) compared with placebo (n=80; IV daily) in combination with SoC in participants with severely reduced kidney function who were hospitalized for COVID-19. Eligible participants had an eGFR <30 mL/min/1.73 m^2, including participants with kidney failure on chronic dialysis or AKI (SCr increase of 50% in the prior 48 hours and sustained for ≥6 hours), and O_2 saturation ≤94% on room air or required supplemental O_2. Participants aged ≥12 years were eligible for study enrollment; however, no participants aged of <18 years enrolled in the study. Participants who required IMV, NIV, ECMO, or dialysis for AKI were not eligible for study enrollment. The primary endpoint was a composite of all-cause mortality or the initiation of IMV through Day 29.

Table 1. REDPINE: Select Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		RDV (n=163)	Placebo (n=80)	*P*-Value
Age, mean ± SD, years		68±14	71±13	0.054
≥65 years, n (%)		93 (57.1)	58 (72.5)	0.02
Male, n (%)		92 (56.4)	47 (58.8)	0.73
Kidney disease status, n (%)	AKI	60 (36.8)	30 (37.5)	0.95
	CKD	44 (27)	20 (25)	
	Kidney failure	59 (36.2)	30 (37.5)	
RRT at baseline,[a] n (%)		40 (24.5)	21 (26.3)	0.77
SCr in participants with AKI, mean ± SD, mg/dL		3.36±1.8	3.45±2.8	0.39
SCr in participants with CKD, mean ± SD, mg/dL		3.28±1.4	2.78±0.8	0.17
Solid organ transplant recipient, n (%)		35 (21.5)	7 (8.8)	0.01
COVID-19 vaccinated, n (%)		21 (12.9)	10 (12.5)	0.93
High-flow O_2 need, n (%)		30 (18.4)	15 (18.8)	0.95

[a]RRT that was utilized ≥3 days prior to RDV initiation or any time after the first dose was not included.

Efficacy[2]

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 by Day 29 (29.4% [n=48] and 32.5% [n=26], respectively; HR, 0.82; 95% CI: 0.5–1.32; *P*=0.61). This remained true regardless of baseline kidney disease status (AKI: HR, 0.84; 95% CI: 0.4–1.77; *P*=0.65; CKD: HR, 0.81; 95% CI: 0.3–2.18; *P*=0.67; kidney failure: HR, 1.06; 95% CI: 0.48–2.36; *P*=0.88). However, due to insufficient enrollment, the study was not powered to determine a difference in efficacy outcomes between the study groups.

There was not a significant difference in the rate of all-cause death by Day 29 between the RDV and placebo groups: 25.2% (n=41) and 28.8% (n=23), respectively (HR, 0.83; 95% CI: 0.5–1.39; *P*=0.39).

Safety

Overall, 131 participants (80.4%) in the RDV group and 62 participants (77.5%) in the placebo group experienced ≥1 AE (Table 2).[2]

Table 2. REDPINE: Safety Results[2]

Safety Parameters, n (%)		RDV (n=163)	Placebo (n=80)
Any AE		131 (80.4)	62 (77.5)
AE related to study drug		13 (8)	3 (3.8)
Grade ≥3 AE		102 (62.6)	49 (61.3)
Grade ≥3 AE related to study drug		2 (1.2)	0
Serious AE		82 (50.3)	40 (50)
Serious AE related to study drug		0	0
AE that led to premature discontinuation of study drug[a]		8 (4.9)[b]	1 (1.3)[c]
Treatment-emergent death[d]		47 (28.8)	23 (28.8)
AEs reported in ≥8% of participants	Hypotension	18 (11)	4 (5)
	Acute respiratory failure	13 (8)	5 (6.3)
	Hyperkalemia	13 (8)	3 (3.8)
	Constipation	12 (7.4)	7 (8.8)
	Respiratory failure	10 (6.1)	10 (12.5)
	Anxiety	5 (3.1)	7 (8.8)
	Hypokalemia	5 (3.1)	7 (8.8)
	Hypertension	4 (2.5)	7 (8.8)

[a]Participants could have had ≥1 AE that led to study drug discontinuation.
[b]Each AE occurred once: AKI, delirium, lipase increased, multiple organ dysfunction syndrome, pneumonia, pyelonephritis acute, renal impairment, sepsis, and subdural hematoma.
[c]Acute pulmonary edema.
[d]Included deaths that occurred between the first dose and last dose +30 days (inclusive).

The proportions of participants who developed new or progressive AKI, required RRT, or died by Day 29 were similar among the RDV and placebo groups, regardless of baseline AKI status (RDV, 33.3% [n=20/60]; placebo, 40%[n=12/30]; *P*=0.32) or baseline CKD status (RDV, 34.1% [n=15/44]; placebo, n=6/20 [30%]; *P*=0.81).[2,4] In participants with baseline AKI or CKD, there was no significant difference between treatment groups in the proportion of participants who had a worsening of AKI, CKD, initiation of RRT, or death by Day 29 (each, *P*>0.05). Among participants who did not require chronic dialysis at baseline, regardless of AKI or CKD status, median SCr levels followed generally similar trends from baseline to Day 29 in both treatment groups.[2]

Subanalysis in kidney transplant recipients[5]

A subanalysis was conducted among SOT recipients (RDV, n/N=35/163 [21%]; placebo, n/N=7/80 [9%]), including 34 participants with a history of kidney transplantation (RDV, n=28 [80%]; placebo, n=6 [86%]), to assess SARS-CoV-2 viral dynamics. At baseline, mean SARS-CoV-2 viral loads were similar between the RDV group (overall, n=127; mean ± SD viral load, 5.9±1.5; kidney transplant recipients, n=23; mean ± SD viral load, 6.4±1.3) and the placebo group (n=54; mean ± SD viral load, 6.2±1.5). Through Day 29, mean SARS-CoV-2 viral loads among RDV-treated participants were higher in kidney transplant recipients than in non-SOT recipients. On Day 14, 3 out of 8 kidney transplant recipients (38%) and 14 out of 20 non-SOT recipients (70%) achieved a viral load ≤LLoQ (3.35 $\log_{10}$ c/mL). Kidney transplant recipients also had a significantly smaller reduction in viral load than non-SOT recipients on Day 7 (*P*=0.025). In a modeling analysis of viral loads by duration of RDV treatment in kidney transplant recipients, a 10-day course of RDV was

predicted to achieve a mean viral load <LLoQ at Day 16 compared with a mean viral load >LLoQ at Day 29 with a 5-day course of RDV.

CATCO: Secondary Analysis of RDV in Participants With Severe Renal Dysfunction

Study design and demographics

The overall CATCO study was a phase 3 open-label, randomized, controlled study at 52 Canadian hospitals as a substudy of the global SOLIDARITY trial. Participants were randomly assigned to receive RDV with SoC (n=634; 200 mg loading dose via IV infusion on Day 1, followed by 100 mg daily via IV infusion on Days 2–10 or until discharge) or SoC alone (n=647). No specific renal dysfunction exclusion criteria were specified, and no dose adjustments were required for renal dysfunction or dialysis.[6]

A post hoc analysis was performed using data from participants who had an eGFR <30 mL/min/1.73 m^2 at randomization, including 34 participants who received RDV and 25 who received SoC. Outcomes assessed in this analysis included all-cause mortality (unadjusted and adjusted for sex and baseline eGFR), AEs, proportion of participants who initiated ventilation or hemodialysis, and Day 5 eGFR.[3]

Table 3. CATCO Post Hoc Analysis: Select Baseline Demographics and Disease Characteristics[3]

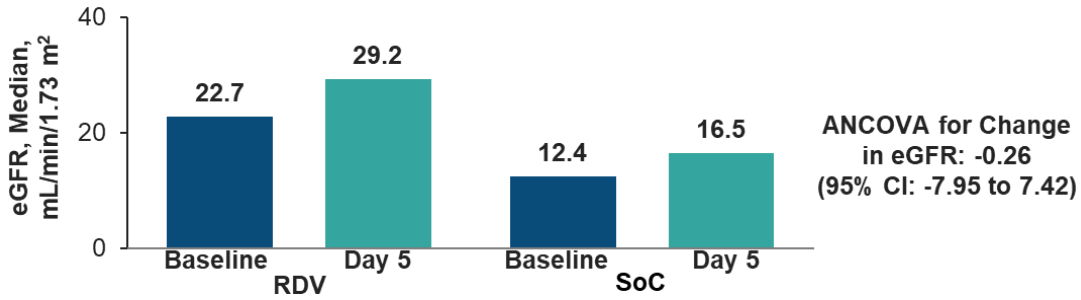
Key Demographics and Characteristics		Overall (N=59)	RDV (n=34)	SoC (n=25)
Age, median (IQR), years		74 (63–86)	74 (66–86)	80 (63–85)
Male, n (%)		30 (50.8)	13 (38.2)	17 (68)
Baseline severity, n (%)	In intensive care unit	18 (30.5)	11 (32.4)	7 (28)
	No O_2	4 (6.8)	4 (11.8)	0
	Receiving O_2	30 (50.8)	16 (47.1)	14 (56)
	High-flow nasal cannula	14 (23.7)	6 (17.6)	8 (32)
	NIV	2 (3.4)	1 (2.9)	1 (4)
	Invasive ventilation	9 (15.3)	7 (20.6)	2 (8)
Cr level, median (IQR), mg/dL		2.97 (2.22–5.54)	2.62 (2.02–5.17)	3.88 (2.65–6.1)
eGFR, median (IQR), mL/min/1.73 m^2		18.9 (10.2–24.2)	22.7 (10.5–26.6)	12.4 (8.8–20.6)
Need for dialysis at baseline, n (%)		15 (25.4)	9 (26.5)	6 (24)

Note: Race and ethnicity data were collected but were not reported due to the small numbers.

Results[3]

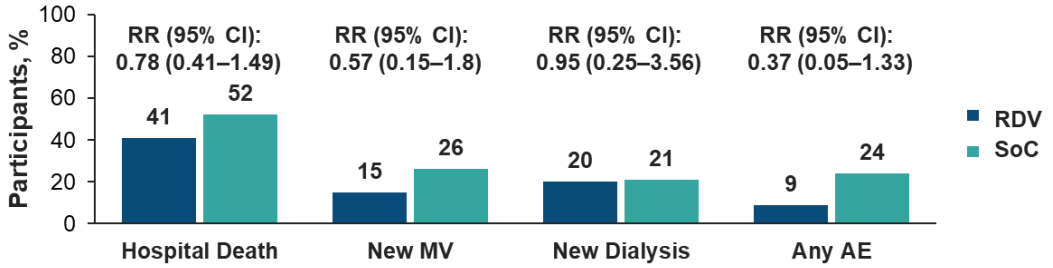
Participants in the RDV group received RDV for a median (IQR) of 10 (6–10) days (mean, 8.2 days). There was no increased risk of eGFR decline at Day 5 (Figure 1), hospital death, AEs, or need for new dialysis or MV with RDV treatment (Figure 2). After an adjustment for sex and baseline eGFR, mortality outcomes were not affected (odds ratio, 0.74; 95% CI: 0.23–2.4).

Figure 1. CATCO Post Hoc Analysis: eGFR at Baseline and Day 5[3]



Abbreviation: ANCOVA=analysis of covariance.
Note: Day 5 eGFR data were available for 45 participants.

Figure 2. CATCO Post Hoc Analysis: Clinical Outcomes[3]



Abbreviation: RR=relative risk.
Note: Percentages are reported for those with available outcome data.

References

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2. Sise ME, Santos JR, Goldman JD, et al. Efficacy and Safety of Remdesivir in People With Impaired Kidney Function Hospitalized for COVID-19 Pneumonia: A Randomized Clinical Trial. *Clin Infect Dis.* 2024;79(5):1172-1181.
3. Cheng M, Fowler R, Murthy S, Pinto R, Sheehan NL, Tseng A. Remdesivir in Patients With Severe Kidney Dysfunction: A Secondary Analysis of the CATCO Randomized Trial. *JAMA Netw Open.* 2022;5(8):e2229236. https://www.ncbi.nlm.nih.gov/pubmed/36036936
4. Sise ME, Santos JR, Goldman JD, et al. Efficacy and Safety of Remdesivir in People With Impaired Kidney Function Hospitalized for COVID-19 Pneumonia: A Randomized Clinical Trial [Supplement]. *Clin Infect Dis.* 2024:1-20.
5. Rodriguez L, Chen S, Hu Y, et al. 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. [Poster #1625]. Paper presented at: IDWeek; October 19-22, 2025; Atlanta, GA.
6. Ali K, Azher T, Baqi M, et al. Remdesivir for the treatment of patients in hospital with COVID-19 in Canada: a randomized controlled trial. *CMAJ.* 2022;194(7):E242-E251.

Abbreviations

AE=adverse event
AKI=acute kidney injury/ impairment
CATCO=Canadian Treatments for COVID-19
CKD=chronic kidney disease
ECMO=extracorporeal membrane oxygenation
HR=hazard ratio
IMV=invasive mechanical ventilation
LLoQ=lower limit of quantification
MV=mechanical ventilation
NIV=non-invasive ventilation
O_2=oxygen
RDV=remdesivir
RRT=renal replacement therapy
SoC=standard of care
SOT=solid organ transplant

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

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

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