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Veklury® (remdesivir) Use in Immunocompromised Patients

This document is in response to your request for information regarding the use of Veklury® (remdesivir [RDV]) in immunocompromised patients. This response was developed according to principles of evidence-based medicine and contains information from phase 3 clinical studies, real-world data, and retrospective studies (N≥500).

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Summary

Clinical Data: RDV Use in Immunocompromised Patients

Currently, there are no clinical trial data available on the use of RDV in immunocompromised patients. Although some clinical trials, such as ACTT-1 and PINETREE, included some immunocompromised participants, efficacy and safety results were not reported for these participants.[1,2]

Retrospective Data: RDV Use in Immunocompromised Patients

In a retrospective, comparative-effectiveness cohort analysis of immunocompromised patients from the PINC AI Healthcare Database who were hospitalized with COVID-19 from December 2021 to February 2024 (Omicron period), the risk of mortality was lower with RDV treatment than without RDV treatment. After adjustment, RDV treatment was associated with lower mortality at Day 14 overall (aHR: 0.75; 95% CI: 0.68–0.83; *P*<0.05) and at Day 28 overall (aHR: 0.78 [95% CI: 0.72–0.86]; *P*<0.05).[3] In another analysis, patients treated with RDV had a lower risk of COVID-19–related readmission at within 30 days of index hospitalization than did those not treated with RDV (OR: 0.86 [95% CI: 0.8–0.92]; *P*<0.0001).[4]

In a PS-matched retrospective cohort study that included patients with mild to moderate COVID-19 who received RDV treatment or no RDV treatment, 29.1% were immunocompromised. In these immunocompromised patients, a treatment benefit was observed with RDV vs no RDV (all-cause hospitalization at Day 28: aOR, 0.31 [95% CI: 0.14–0.66]).[5]

Clinical Data: RDV Use in Immunocompromised Patients

NIAID-Sponsored Study: ACTT-1

A phase 3, randomized, adaptive, double-blind, placebo-controlled, multicenter study evaluated the safety and efficacy of RDV (n=541) vs placebo (n=521) in hospitalized adult

participants diagnosed with COVID-19 with evidence of lower respiratory tract infection.[6] Immune system disorder (definition not provided) was noted as a comorbidity in 32 (6%) and 41 (8%) participants in the RDV and placebo groups, respectively. Efficacy and safety results were not provided for this subset of participants.[1]

RDV IV Outpatient Study: PINETREE

A phase 3, randomized, double-blind, placebo-controlled, multicenter study evaluated the safety and efficacy of a 3-day course of RDV (n=279) or placebo (n=283) administered IV in an outpatient setting in nonhospitalized participants with baseline characteristics that increased their risk for COVID-19 disease progression. Risk factors for progression included immunocompromised status, defined as having undergone an SOT, a blood transplant, or a bone marrow transplant; immune deficiencies; HIV with a low CD4 cell count or not currently receiving HIV treatment; long-term use of corticosteroids; or use of immune-weakening medications.[2,7]

Overall, 14 participants (5%) in the RDV group and 9 participants (3.2%) in the placebo group were immunocompromised; 12 (4.3%) and 18 (6.4%) participants in the RDV and placebo groups, respectively, had cancer.[2] Efficacy and safety results were not provided for these participants.

Retrospective Data: RDV Use in Immunocompromised Patients

Retrospective, Comparative-Effectiveness Cohort Studies: PINC AI Healthcare Database

Immunocompromised patient cohort: analysis of all-cause in-hospital mortality[3]

A retrospective, comparative-effectiveness cohort study evaluated all-cause in-hospital mortality at Days 14 and 28 in immunocompromised patients with a primary discharge diagnosis of COVID-19 (present on admission) during the Omicron period (December 2021–February 2024) who were treated with RDV within 2 days of admission as well as in those who were not treated with RDV during their hospitalization. Immunocompromised states included cancer, SOT, HSCT, hematologic malignancies, primary immunodeficiency, severe combined immunodeficiency, receiving immunosuppressive medications, asplenia, bone marrow failure/aplastic anemia, HIV, or experiencing toxic effects of antineoplastics. Data were obtained from the US-based PINC AI Healthcare Database (formerly known as the Premier Healthcare Database), and patients were PS-matched (1:1 matching with replacement, each PS-matched cohort, n=8822) by baseline supplemental O_2 requirement, which was determined within the first 2 days of hospitalization. In the overall matched cohort at baseline, 77% of patients were ≥65 years of age, and 54% did not have supplemental O_2 needs.

Results

In the PS-matched cohort, patients treated with RDV had lower unadjusted 14- and 28-day mortality rates overall. In addition, lower unadjusted mortality rates were observed in

patients with and those without supplemental O_2 needs in the RDV cohort, compared with the no RDV cohort (Table 1).

In an adjusted analysis (for age, admission month, intensive care unit vs general ward, and baseline treatments), RDV treatment was associated with lower mortality at Day 14 overall (P<0.0001) and at Day 28 overall (P<0.0001), compared with no RDV treatment. In the RDV cohort, compared with the no RDV cohort, lower 14- and 28-day mortality risks were also observed in subgroups of patients with no supplemental O_2 needs and with any supplemental O_2 needs (Table 1).

Table 1. PS-Matched Cohort: Unadjusted All-Cause Mortality Rates and Adjusted Risk of Mortality at Days 14 and 28 Overall and by Baseline O_2 Requirements[3,8]

Mortality, n (%)	Day 14			Day 28		
	RDV	No RDV	aHR (95% CI)[a]	RDV	No RDV	aHR (95% CI)[a]
Overall	813 (9.2)	1044 (11.8)	0.75 (0.68–0.83)	1120 (12.7)	1362 (15.4)	0.78 (0.72–0.86)
No supplemental O_2	276 (5.8)	365 (7.6)	0.73 (0.62–0.86)	380 (8)	462 (9.7)	0.79 (0.68–0.91)
Any supplemental O_2	537 (13.3)	679 (16.8)	0.75 (0.67–0.85)	740 (18.3)	900 (22.2)	0.78 (0.7–0.86)

[a]Each P-value, <0.05. Values <1 favor RDV, whereas values >1 favor no RDV.

RDV was associated with significantly lower mortality at Days 14 and 28 across several prespecified immunosuppressive conditions (Table 2); however, the treatment benefit with RDV was not significant at Day 14 in those with lymphoma. The mean length of RDV treatment overall and in the patient subgroups noted below was 4.1 and 4.2 days, respectively.

Table 2. PS-Matched Cohort: Unadjusted All-Cause Mortality Rates and Adjusted Risk of Mortality at Days 14 and 28 in Select Underlying Immunosuppressive Conditions[3]

Mortality, %	Day 14			Day 28		
	RDV	No RDV	aHR (95% CI)	RDV	No RDV	aHR (95% CI)[a]
Cancer	12	16	0.73 (0.66–0.8)[a]	15.5	20.1	0.74 (0.68–0.81)
Hematologic malignancy	10.3	15.9	0.62 (0.52–0.74)[a]	14.1	21.2	0.64 (0.54–0.74)
Leukemia	11.5	17.9	0.61 (0.47–0.79)[a]	14.7	21.4	0.65 (0.51–0.83)
Lymphoma	10.6	13.7	0.78 (0.58–1.04)	15.2	20.8	0.72 (0.56–0.92)
Multiple myeloma	7.2	16.5	0.39 (0.25–0.61)[a]	10.6	22	0.41 (0.28–0.61)
SOT and HSCT recipients	5	8	0.64 (0.44–0.95)[a]	7.9	12.2	0.65 (0.48–0.87)[a]

[a]Each P-value, <0.05. Values <1 favor RDV, whereas values >1 favor no RDV.

Immunocompromised patient subgroup: COVID-19–related readmission

Another retrospective analysis evaluated the association between RDV treatment and COVID-19–related readmission at within 30 days of index hospitalization in patients admitted for COVID-19 who were discharged alive between December 2021 and February 2024. One of the subgroup analyses included patients with immunocompromised conditions, and they were further categorized according to the need for supplemental O_2.[4] Among those in the immunocompromised subgroup (RDV, n=18,542; no RDV, n=14,775), after IPTW, 70% were ≥65 years of age, ~79% received corticosteroids, ~50% did not require supplemental O_2 during their initial admission, and ~40% had cancer.[4,9]

At readmission, the mean ± SD length of stay was 8.9±13.2 days and the all-cause in-hospital mortality rate was 26%; 55% received corticosteroid monotherapy, 12% received RDV + corticosteroids, 5% received RDV + corticosteroids + baricitinib/tocilizumab, 3% received RDV + corticosteroids/baricitinib/tocilizumab, and 1% received RDV monotherapy.

There was a 14% lower risk of COVID-19–related readmission with RDV than without RDV (5.3% vs 6.2%; OR: 0.86 [95% CI: 0.8–0.92]; *P*<0.0001). Regardless of the need for supplemental O_2, similar outcomes were noted for RDV vs no RDV: no supplemental O_2, 4.9% vs 5.9% (OR: 0.82 [95% CI: 0.75–0.91]); supplemental O_2, 5.8% vs 6.5% (OR: 0.89 [95% CI: 0.81–0.97]).[4]

Analysis by VOC period: mortality analyses[10]

Data from pre-Delta (December 2020–April 2021), Delta (May–November 2021), and Omicron (December 2021–April 2022) VOCs have been previously published; significantly lower mortality risks were associated with RDV treatment over no RDV treatment and were observed across each VOC period. In subgroup analyses according to baseline O_2 requirement, numerically lower mortality rates were observed with RDV treatment than without RDV treatment.

Retrospective Cohort Study in Non-Hospitalized Patients[5]

A PS-matched retrospective cohort study compared all-cause hospitalization within 28 days of the index date (defined as the date of positive SARS-CoV-2 test, if available) between outpatients with mild to moderate COVID-19 who were treated with RDV and those who were not. Included were those who had laboratory-confirmed SARS-CoV-2 infection or had received ≥1 outpatient RDV dose between April 2022 and February 2023, which was an Omicron-predominant period. Data were obtained from the University of Colorado and Colorado Department of Public Health and Environment electronic health records, and patients were PS-matched (1:2 matching; PS-matched cohort: RDV, n=1252; no RDV, n=2499). Overall, 29.1% were immunocompromised; in the RDV and no RDV cohorts, 13.7% and 13%, respectively, had mild immunocompromised status; 16.6% and 15.5%, respectively, had moderate/severe immunocompromised status. Approximately half of the patients were aged ≥65 years (47.7%) and had ≥2 comorbid conditions (48.3%).

Results

In the PS-matched cohort, patients treated with RDV had a significant reduction in all-cause hospitalization by Day 28 relative to those who did not receive RDV (primary endpoint); similarly, the rate of COVID-19–related hospitalizations by Day 28 was significantly lower in the RDV cohort than in the no RDV cohort (key secondary endpoint). The rate of ED visits by Day 28 was numerically higher in the RDV cohort than in the no-RDV cohort; however, the mortality rate by Day 28 was 68% lower in the RDV cohort than in the no RDV cohort, although this difference was not significant (Table 3).

Table 3. Outcomes by Day 28 in PS-Matched Cohort (Molina et al)[5]

Outcomes at Day 28, n (%)	RDV Cohort (n=1252)	No RDV Cohort (n=2499)	aHR or aOR (95% CI); *P*-Value
All-cause hospitalization	16 (1.3)	82 (3.3)	aHR: 0.39 (0.23–0.67); <0.001
COVID-19–related	14 (1.1)	76 (3)	aOR: 0.37 (0.2–0.63); <0.001
All-cause ED visit	95 (7.6)	162 (6.5)	aOR: 1.18 (0.9–1.54); 0.23
All-cause mortality	1 (0.1)	10 (0.4)	aOR: 0.32 (0.03–1.4); 0.15

Note: Data were adjusted for age, sex, race/ethnicity, obesity, immunocompromised status, number of comorbidities, insurance status, vaccination status, and subvariant period.

In prespecified subgroup analyses, a treatment benefit was observed with RDV vs no RDV in those with any immunocompromised status (Table 4).

Table 4. Subgroup Analyses of All-Cause Hospitalization by Day 28: According to Immunocompromised Status (Molina et al)[5]

Immunocompromised Status, n/N (%)		RDV Cohort	No-RDV Cohort	aOR (95% CI)
Binary assessment	No	9/873 (1)	37/1788 (2.1)	0.51 (0.23–0.99)
	Yes	7/379 (1.9)	45/711 (6.3)[a]	0.31 (0.14–0.66)
Variable assessment	Mild	4/171 (2.3)	15/324 (4.6)	0.61 (0.21–1.75)
	Moderate-severe	3/208 (1.4)	30/387 (7.8)[a]	0.2 (0.07–0.59)

[a]*P*-values for interaction within subgroups, each >0.05.

References

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Abbreviations

ACTT-1=Adaptive COVID-19 Treatment Trial-1
aHR=adjusted hazard ratio
aOR=adjusted odds ratio
CD4=cluster of differentiation 4
ED=emergency department
HSCT=hematopoietic stem cell transplantation
IPTW=inverse probability of treatment weighting
NIAID=National Institute of Allergy and Infectious Diseases
O_2=oxygen
OR=odds ratio
PINC AI=Premier Inc. Artificial Intelligence
PS=propensity score
RDV=remdesivir
SOT=solid organ transplantation
VOC=variants of concern

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

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