GILEAD | Medical Information

Veklury® (remdesivir) Use in Pediatric Patients

This document is in response to your request for information regarding the use of Veklury® (remdesivir [RDV]) in pediatric patients for the treatment of COVID-19. This response was developed according to principles of evidence-based medicine and contains data from phase 2/3 clinical studies.

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]

RDV is indicated for the treatment of COVID-19 in adults and pediatric patients (birth to <18 years of age weighing at least 1.5 kg) who are hospitalized or not hospitalized, have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

Use of RDV in pediatric patients from birth to <18 years of age and weighing ≥1.5 kg is supported by Study 5823, where 58 hospitalized pediatric participants were treated with weight-based RDV for up to 10 days.

The safety and pharmacokinetic results in pediatric participants were similar to those in adults (see Adverse Reactions [Section 6.1], Clinical Pharmacology [Section 12.3], Clinical Studies [Section 14.6]).

Please refer to Section 8.4 Pediatric Use in the US Prescribing Information for complete information.

Clinical Data on the Use of RDV in Pediatric Patients

CARAVAN Pediatric Study: An analysis of 53 hospitalized pediatric participants (age <18 years) who received RDV showed that clinical status improved in 75% of participants at Day 10 and in 85% of participants at the last study assessment; 60% and 83% of participants were discharged by Days 10 and 30, respectively. No new safety signals were observed, and RDV was well tolerated.[2]

PINETREE (Outpatient Study): Eight non-hospitalized participants aged <18 years were included in this study (RDV, n=3; placebo, n=5), and none had experienced a COVID-19–related hospitalization or death by Day 28.[3] Of the participants aged <18 years, 1 participant in the placebo group had an AE of mild fatigue.[4]

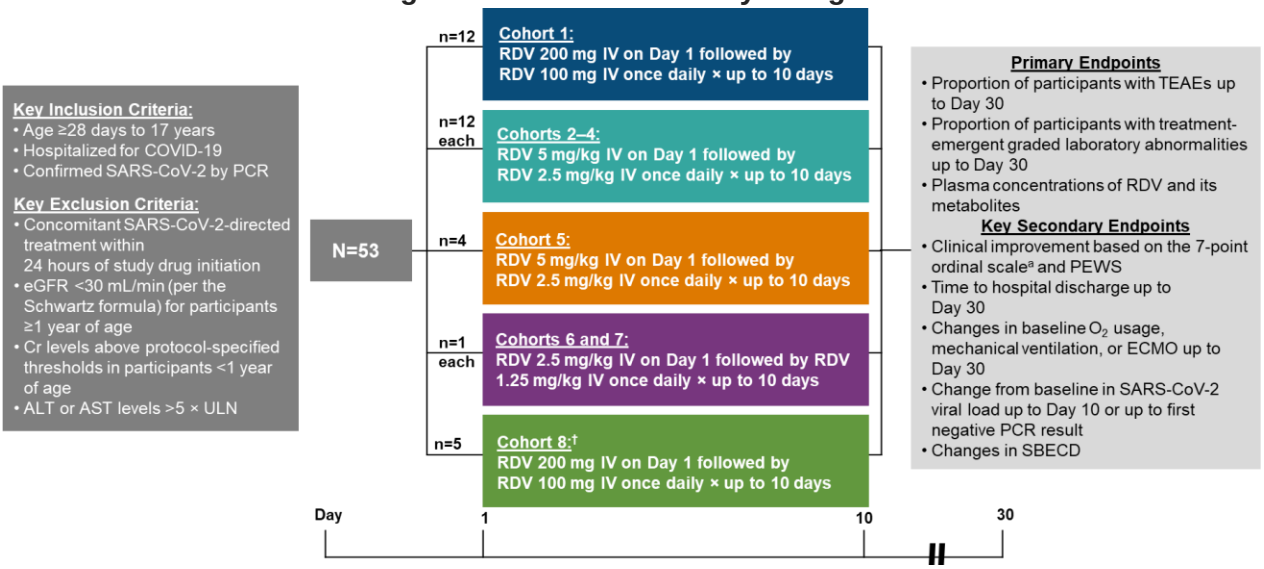
Clinical Data on the Use of RDV in Pediatric Patients

CARAVAN Study: RDV in Pediatric Participants Hospitalized With COVID-19

Study design

A phase 2/3, single-arm, open-label study (GS-US-540-5823, NCT04431453 and EudraCT 2020-001803-17) in the US and Europe evaluated the safety, tolerability, PK, and efficacy of RDV in pediatric participants aged ≥28 days to 17 years, weighing ≥3 kg, and hospitalized with COVID-19 (Figure 1). The primary endpoints were as follows: proportion of participants experiencing any TEAEs, proportion of participants experiencing treatment-emergent laboratory abnormalities, and plasma concentrations of RDV and its metabolites.[2]

Figure 1. CARAVAN: Study Design[2,5]



Abbreviations: PCR=polymerase chain reaction; PEWS=Pediatric Early Warning Score; SBECD=sulfobutylether β-cyclodextrin; ULN=upper limit of normal.

[a]Clinical status is assessed using a 7-point ordinal scale: 1) death; 2) hospitalized and requires IMV or ECMO; 3) hospitalized and requires non-invasive ventilation or high-flow O_2 devices; 4) hospitalized and requires low-flow supplemental O_2; 5) hospitalized and does not require supplemental O_2 but requires ongoing medical care (COVID-19–related or otherwise); 6) hospitalized but does not require supplemental O_2 or ongoing medical care (other than RDV administration); 7) not hospitalized.

Participant demographics and disposition for Cohorts 1 Through 4, 8[2]

An assessment of 53 participants enrolled in Cohorts 1 through 4 and 8 from July 2020 to May 2021 was conducted. Overall, the median treatment duration was 5 days. The most common reasons for a treatment duration <10 days were hospital discharge (42%) and investigator discretion (25%). Among the 53 participants, the mean (IQR) age was 7 (2–12) years; the median (IQR) weight was 25 (13–55) kg; 57% were assigned female at birth; racial makeup consisted of 33 (70%) White participants, 14 (30%) Black participants, and 23 (44%) Hispanic/Latinx participants. Medical conditions included obesity in 19 (37%) participants, cardiac disorders in 11 (21%), and asthma in 11 (21%).

Primary endpoints: safety results for Cohorts 1 Through 4, 8[2]

Overall, 38 participants (72%) experienced ≥1 AE during the study; ≥Grade 3 AEs were reported in 15 participants (28%). No treatment-related SAEs were reported. Overall, 2 (4%) treatment discontinuations due to AEs were reported, and 3 (6%) deaths occurred that were considered unrelated to study drug (Table 1).

Table 1. CARAVAN: Primary Safety Results[2]

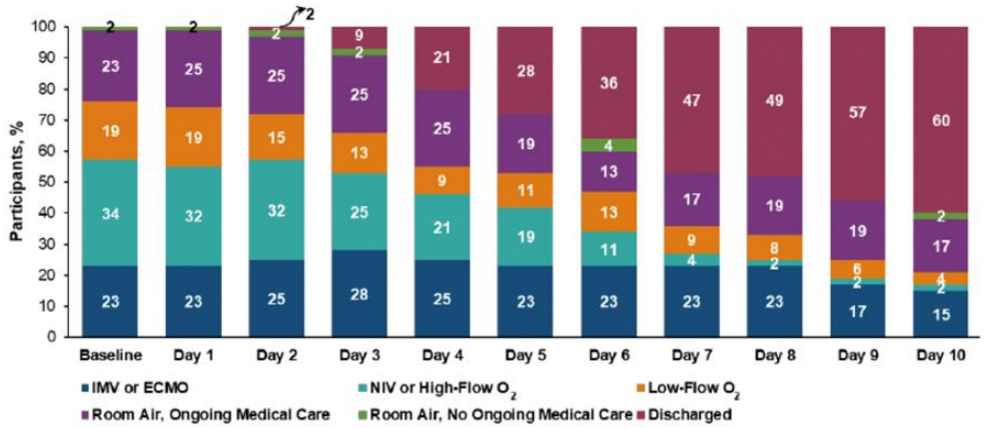
AEs	Total (N=53)	Cohort 1: ≥40 kg and 12 to 17 y (n=12)	Cohort 2: 20 to <40 kg and 28 d to 17 y (n=12)	Cohort 3: 12 to <20 kg and 28 d to 17 y (n=12)	Cohort 4: 3 to <12 kg and 28 d to 17 y (n=12)	Cohort 8: ≥40 kg and <12 y (n=5)
Any AE, n (%)	38 (72)	11 (92)	7 (58)	9 (75)	7 (58)	4 (80)
AEs that occurred in ≥9% of participants overall, n (%)						
Constipation	9 (17)	3 (25)	1 (8)	1 (8)	1 (8)	3 (60)
AKI	6 (11)	4 (33)	0	0	1 (8)	1 (20)
Hyperglycemia	5 (9)	1 (8)	1 (8)	1 (8)	2 (17)	0
Pyrexia	5 (9)	1 (8)	2 (17)	1 (8)	1 (8)	0
Any Grade ≥3 AEs, n (%)	15 (28)	6 (50)	2 (17)	1 (8)	4 (33)	2 (40)
Treatment-related Grade ≥3 AEs, n (%)	3 (6)	3 (25)	0	0	0	0
SAEs,[a] n (%)	11 (21)	5 (42)	2 (17)	0	3 (25)	1 (20)
Treatment-related SAEs, n (%)	0	0	0	0	0	0
Treatment discontinuation due to an AE,[b] n (%)	2 (4)	2 (17)	0	0	0	0
Death,[c] n (%)	3 (6)	1 (8)	1 (8)	0	0	1 (20)
Laboratory abnormalities						
Grade 3–4, n (%)	22 (42)	9 (75)	2 (17)	4 (33)	4 (36)	3 (60)

[a]Included cardiorespiratory arrest, multiple organ dysfunction syndrome, pyrexia, respiratory distress, septic shock, and thrombosis (each, n=2).
[b]Grade 3 ALT increase (n=1); Grade 4 hyperbilirubinemia, Grade 3 ALT increase, Grade 3 AST increase, and Grade 4 increased serum sodium level (all in 1 participant). Both participants had elevated transaminase levels at baseline.
[c]Immediate causes of death included multisystem organ failure and cardiorespiratory arrest, among others. No deaths were treatment related. One additional participant died 32 days after the last dose of RDV.

Secondary endpoints: efficacy results for Cohorts 1 Through 4, 8[2]

Overall, 60% of participants (32/53) were discharged by Day 10, and 83% of participants (44/53) were discharged by Day 30. Among participants who were discharged alive by Day 30, the median (IQR) duration of hospitalization from Day 1 of RDV was 7 (5–12) days. Additionally, 75% and 85% of participants showed clinical improvement (defined as a ≥2-point increase in ordinal score from baseline) at Day 10 and at the last clinical assessment, respectively. The overall recovery rate was 83% (improvement from a baseline ordinal score of 2–5 to score of 6 or 7 or from a baseline score of 6 to a score of 7).

Figure 2. CARAVAN: Clinical Status Results According to Ordinal Scale by Study Day[2]



Interim Results for Cohorts 5 Through 7[1]

Cohort 5 included participants who were 14 to <28 days old, GA >37 weeks, and weighed ≥2.5 kg (n=3). Cohorts 6 and 7 included participants who were <14 days old, GA >37 weeks, and weighed ≥2.5 kg at birth (n=1); and <56 days old, GA ≤37 weeks, and weighed ≥1.5 kg at birth (n=1), respectively. At baseline, participants were 12 to 30 days old, 3/5 were female, 4/5 were White, 1/5 were Black, and weight ranged from 2.2 to 3.5 kg. Three participants were on IMV and 2 were on high-flow O_2. Symptom duration prior to first RDV dose was 2 to 9 days.

Among the neonate and infant participants in Cohorts 5 through 7, laboratory abnormalities (Grades 3–4) were reported in 3/5 participants and included APTT increased (2/5), direct bilirubin increased (1/5), creatinine increased (1/5), prothrombin time increased (1/5), prothrombin/INR increased (1/5), and potassium increased (1/5).

Three participants who received RDV recovered, including one participant who recovered by Day 10. Time to recovery ranged from 9 to 19 days. Overall, 3 participants were discharged by Day 30; one of these participants was discharged by Day 10. No participants from Cohorts 5 through 7 died during the study.

PINETREE Outpatient Study: RDV in Non-hospitalized Participants With COVID-19

Study design

A phase 3, randomized, double-blind, placebo-controlled, multicenter study that enrolled 584 participants evaluated the safety and efficacy of a 3-day course of RDV administered in an outpatient setting in non-hospitalized participants with baseline characteristics that increased their risk for COVID-19 disease progression. Participants received RDV 200 mg IV on Day 1 and RDV 100 mg IV daily on Days 2 and 3. Participants in the placebo group received IV placebo daily on Days 1 to 3. Participants could receive study treatment at outpatient infusion facilities, skilled nursing facilities, or at their home.[3,6] The primary efficacy endpoint was the composite of COVID-19–related hospitalizations (defined as ≥24 hours of acute care; determined by site investigators who were blinded regarding treatment assignments) or all-cause death by Day 28.[3]

Participant demographics and disposition

Among the overall study population, there were 8 participants aged <18 years included in the study (RDV, n=3; placebo, n=5). All pediatric participants were White; the median (IQR) ages in the RDV and placebo groups were 13 (13–17) years and 16 (15–16) years, respectively, and the median (IQR) BMI in the RDV and placebo groups were 25.7 (21.1–31.7) kg/m^2 and 28.7 (23.2–29.1) kg/m^2, respectively.[3,4]

Efficacy

In the overall study population, treatment with RDV in comparison with placebo was associated with an 87% reduction in the risk of COVID-19–related hospitalization or all-cause death by Day 28 (HR: 0.13; 95% CI: 0.03–0.59; *P*=0.008). No pediatric participants aged <18 years had experienced a COVID-19–related hospitalization or death by Day 28.[3]

Safety

In the overall study population by Day 28, the safety profile of RDV was similar to that of placebo.[3,4] Of the 8 pediatric participants aged <18 years, 1 participant in the placebo group had an AE of mild fatigue. None of the 8 pediatric participants in either group reported study drug-related AEs; SAEs; AEs that led to drug discontinuation, hospitalization, or death; or Grade ≥3 laboratory abnormalities.[4]

References

1. VEKLURY®, Gilead Sciences Inc. Veklury® (remdesivir) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Ahmed A, Munoz FM, Muller WJ, et al. Remdesivir for COVID-19 in Hospitalized Children: A Phase 2/3 Study. *Pediatrics.* 2024;153(3):e2023063775.
3. Gottlieb RL, Vaca CE, Paredes R, et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. *N Eng J Med.* 2022;386(4):305-315.
4. Webb B, Oguchi G, Sachdeva Y, et al. Safety of Remdesivir vs Placebo in Nonhospitalized Patients With COVID-19 [Poster 456]. Paper presented at: Virtual Conference on Retroviruses and Opportunistic Infections (CROI) 2022; 12-16 February, 2022.
5. ClinicalTrials.gov. Study of Remdesivir in Participants Below 18 Years Old With COVID-19 (CARAVAN) Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04431453 Accessed: 14 May 2024. Last Updated: 06 February. 2024.
6. Gottlieb RL, Vaca CE, Paredes R, et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients [Protocol]. *N Eng J Med.* 2021.

Abbreviations

AE=adverse event(s)
AKI=acute kidney injury
APTT=activated partial thromboplastin time
CARAVAN=Clinical Administration of Remdesivir After COVID-19 Diagnosis in Children
ECMO=extracorporeal membrane oxygenation
GA=gestational age
HR=hazard ratio
IMV=invasive mechanical ventilation
NIV=non-invasive ventilation
O_2=oxygen
PK=pharmacokinetic(s)
RDV=remdesivir
SAE=serious adverse event
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
🖱 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

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