GILEAD | Medical Information

Veklury® (remdesivir) Use in Patients With Ebola

This document is in response to your request for information regarding the use of Veklury® (remdesivir [RDV]) in patients with Ebola virus disease (EVD).

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.

Veklury is not indicated for use in patients with Ebola. 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 ≥1.5 kg) who are hospitalized or not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

Available Data on RDV Use in Patients With Ebola

The PALM study in the DRC compared the efficacy and safety of RDV, ZMapp, MAb114, and REGN-EB3 as treatment for EVD (N=673). At the interim analysis, higher efficacy was noted in the MAb114 and REGN-EB3 arms than in the RDV and ZMapp arms; thus, the data safety monitoring board recommended halting assignment to the RDV and ZMapp arms. Nine SAEs were reported in the RDV arm, including 1 SAE of hypotension that resulted in death and was assessed as potentially related to study drug.[2]

In a retrospective cohort study that used data from the National Institute of Public Health in the DRC (N=784), treatment with RDV was associated with a significantly lower risk of mortality than SOC treatment (aHR, 0.38; *P*=0.005).[3]

Available Data on RDV Use From Animal Studies

In a study that assessed RDV ± MBP431 use in rhesus macaques infected with SUDV, there was a significant survival difference between rhesus macaques treated with RDV + MBP431 and the combined in-study and historical control group (*P*=0.038) and untreated controls (*P*=0.014). There was no significant survival difference between macaques who received either RDV monotherapy or MBP431 monotherapy and untreated controls (*P*=0.479 and *P*=0.088, respectively).[4]

Available Data on RDV Use in Patients With Ebola

PALM Study

Study design and demographics[2]

The PALM study was a multicenter study in the DRC that compared the efficacy and safety of RDV, ZMapp, MAb114, and REGN-EB3 in participants with EVD (N=673). Eligible participants were any age, tested positive for Ebola virus by RT-PCR within 3 days of screening, and had not received other investigational agents within the past 30 days. In addition to receiving SOC, participants were randomly assigned 1:1:1:1 to receive RDV (in adults, Day 1 loading dose of 200 mg IV, followed by a maintenance dose of 100 mg beginning on Days 2, and continued for up to 9 to 13 days, depending on viral load; pediatric doses were adjusted for body weight), ZMapp (50 mg/kg of body weight once every 3 days for a total of 3 doses), MAb114 (50 mg/kg as a single IV infusion), or REGN-EB3 (150 mg/kg as a single IV infusion). The primary endpoint was death at 28 days.

Overall, 55.6% of participants were female (including 6.1% who were pregnant at EVD diagnosis), 74.4% were aged ≥18 years, and the average duration from onset of symptoms to enrollment was 5.5 days. The mean baseline AST and SCr levels were higher in the RDV (AST, 713 U/L; SCr, 2.7 mg/dL) and ZMapp (AST, 767 U/L; SCr, 2.9 mg/dL) arms than in the MAb114 (AST, 546 U/L; SCr, 2.1 mg/dL) and REGN-EB3 (AST, 648 U/L; SCr, 2.5 mg/dL) arms; however, baseline AST and SCr levels were not recorded in 40.6% and 18.6% of participants, respectively.

Results

At the interim analysis (August 9, 2019), higher efficacy was noted in the MAb114 and REGN-EB3 arms than in the RDV and ZMapp arms; thus, the data safety monitoring board recommended halting assignment to the RDV and ZMapp arms. At 28 days, death had occurred in 290/673 participants (43.1%) overall, including 93/175 participants (53.1%) who received RDV, 84/169 (49.7%) who received ZMapp, 61/174 (35.1%) who received MAb114, and 52/155 (33.5%) who received REGN-EB3. Relative to ZMapp, the treatment difference for mortality with RDV was 3.4% (95% CI: -7.2 to 14%). Compared with other treatments, RDV treatment was associated with a higher incidence of death among participants with both a high viral load (Ebola nucleoprotein Ct ≤22: 64/75 [85.3%]) and a low viral load (Ebola nucleoprotein Ct >22: 29/100 [29%]) at baseline.[2]

Nine SAEs were reported in the RDV arm; 8 were assessed as not related to treatment, and 1 SAE of hypotension that resulted in death was assessed by a pharmacovigilance working group as potentially related to study drug.[2,5]

Retrospective Cohort Study[3]

Study design and demographics

A retrospective cohort study used data from the National Institute of Public Health in the DRC to compare the effectiveness and safety of RDV, MAb114, REGN-EB3, and ZMapp treatment with those of SOC in patients with EVD (N=784). The primary outcome measure was 28-day mortality, as assessed by Kaplan-Meier method. A Cox regression model was used to identify factors associated with survival, such as treatment arm, vaccine status, and the interaction of these two factors.

Overall, 243 patients (31%) received REGN-EB3, 215 (27%) received MAb114, 167 (21%) received RDV, 104 (13%) received ZMapp, and 55 (7%) received SOC. The mean age was 29.43 years, 58.3% were female, and 53.9% were unvaccinated. Baseline demographics and characteristics were generally comparable between treatment groups; however, more patients in the SOC group were unvaccinated than in other treatment groups, and vaccinated patients had a shorter duration between symptom onset and hospital admission than unvaccinated patients (3.7 days vs 5 days, respectively; *P*=0.0002).

Results

The mortality rate was lower among patients who received MAb114, RDV, and REGN-EB3 than in those who received SOC. Among the 167 patients who received RDV, death was reported in 77 patients over the course of 1915 days (incidence rate, 40.2 per 1000 patient days). Compared with SOC treatment, treatment with RDV was associated with a significantly lower risk of mortality (aHR, 0.38; *P*=0.005). Overall, patients who had received the Ebola vaccine were 1.7 times less likely to die than patients who had not received the vaccine (relative risk, 0.59), regardless of which treatment they received (aHR, 0.57; *P*=0.003).

Additional safety data were not reported.

Available Data on RDV Use From Animal Studies

RDV ± MBP431 Treatment for SUDV in Rhesus Macaques[4]

Two studies assessed the efficacy of RDV ± MBP431 in rhesus macaques infected with SUDV (Gulu variant). In the first study, 6 healthy adult rhesus macaques were challenged with a target dose of 1000 PFU of SUDV by intramuscular injection. Five days post-infection, the experimental cohort (n=5) then received a 10 mg/kg IV loading dose of RDV, followed by 5 mg/kg daily maintenance doses for 12 days; the remaining rhesus macaque served as the positive control. All rhesus macaques developed fevers by 5 days post-infection; 2 rhesus macaques progressed to severe EVD and required humane euthanasia at post-infection Days 7 and 9, 2 developed severe clinical symptoms before regaining health, and 1 had mild symptoms. The rhesus macaque that served as the control was euthanized at post-infection Day 7. The difference in survival was not statistically significant between the RDV-treated cohort and the control cohort, which included the 1 control and 9 historical controls (*P*=0.063). All macaques exhibited marked changes from baseline in hematological and serum markers, which returned to near-baseline values in surviving macaques.

In the next study, the efficacy of RDV monotherapy (n=5), MBP431 monotherapy (n=5), and RDV + MBP431 (n=5; single dose of MBP431 15 mg/kg IV in tandem with a 12-day course of RDV) was assessed in rhesus macaques, with treatment initiation on post-infection Day 6; 1 rhesus macaque served as control. The control rhesus macaque developed clinical signs of EVD on post-infection Day 5 and reached a clinical score that required humane euthanasia on post-infection Day 6. In both the RDV monotherapy and MBP431 monotherapy groups, survival was low, with only 1/5 (20%) macaques in each cohort surviving to the study endpoint 35 days post-infection (mean time to death, 8.8 days and 10.5 days, respectively). In the RDV + MBP431 group, 4/5 rhesus macaques (80%) survived to the study endpoint. There was a significant survival difference between rhesus macaques treated with RDV + MBP431 the combined in-study and historical control group (*P*=0.038) and untreated control in-study (*P*=0.014). Both surviving macaques in the RDV monotherapy

and MBP431 monotherapy groups developed severe clinical signs of EVD, while 2 macaques in the RDV + MBP431 group only had mild symptoms There was no significant survival difference between macaques who received either RDV monotherapy or MBP431 monotherapy and untreated controls (*P*=0.479 and *P*=0.088, respectively). All macaques exhibited marked changes from baseline in hematological and serum laboratory values at 6 days post-infection that were consistent with SUDV infection in macaques. Most marker returned to near-baseline values by 12 days post-infection, while some markers (ie, ALT, AST, ALP, GGT) remained slightly elevated among surviving macaques in the RDV-monotherapy group.

References

1. Veklury, Gilead Sciences Inc. VEKLURY® (remdesivir) for injection, for intravenous use. U. S. Prescribing Information. Foster City, CA.
2. Mulangu S, Dodd LE, Davey RT, Jr., et al. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. *N Engl J Med.* 2019;381(24):2293-2303.
3. Kikwango EM, Akilimali PZ, Tran NT. Impact of most promising Ebola therapies on survival: a secondary analysis during the tenth outbreak in the Democratic Republic of Congo. *Virol J.* 2025;22(1):144.
4. Cross RW, Bornholdt ZA, Prasad AN, et al. Combination therapy with remdesivir and monoclonal antibodies protects nonhuman primates against advanced Sudan virus disease. *JCI Insight.* 2022;7(10):e159090.
5. Mulangu S, Dodd LE, Davey RT, Jr., et al. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics [Supplementary Appendix]. *N Engl J Med.* 2019;381(24):2293-2303.

Abbreviations

aHR=adjusted hazard ratio
DRC=Democratic Republic of Congo
EVD=Ebola virus disease
MAb114=single human monoclonal antibody derived from an Ebola survivor
MBP431=pan-Ebolavirus monoclonal antibody cocktail
PALM=Pamoja Tulinde Maisha
RDV=remdesivir
REGN-EB3=coformulated mixture of three human IgG1 monoclonal antibodies
PFU=plaque-forming unit
RT-PCR=reverse transcriptase polymerase chain reaction
SAE=serious adverse event
SOC=standard of care
SUDV=Sudan virus
ZMapp=a triple monoclonal antibody agent

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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