GILEAD | Medical Information

Veklury® (remdesivir) Solidarity Study

This document is in response to your request for information regarding the Solidarity study, which evaluated the safety and efficacy of Veklury® (remdesivir [RDV]) and other potential therapies in comparison to standard of care in participants hospitalized with COVID-19.

Please note that this document only summarizes the data obtained from the RDV and accompanying control groups, as the other active comparator groups were discontinued.

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

Clinical Data From the Solidarity Study

The Solidarity study was a randomized, open-label, phase 3 clinical trial that compared the safety and efficacy of four treatment options (RDV, hydroxychloroquine, LPV/r, and IFN-β1a) with local SoC (control group). The primary endpoint was the in-hospital mortality rate.[1]

- Overall, mortality rates were not significantly lower with RDV than control (14.5% (602/4146) and 15.6% (643/4129), respectively (RR, 0.91; 95% CI: 0.82–1.02; *P*=0.12; Figure 2).
- Compared with the control group, treatment with RDV was associated with decreased mortality among nonventilated participants (11.9% vs 13.5%, respectively; RR, 0.86; 95% CI: 0.76–0.98; *P*=0.02; Figure 3).
- Fewer participants in the RDV group than the control group met the non-prespecified composite outcome of death or ventilation initiation (19.6% vs 22.5%, respectively; RR, 0.84; 95% CI: 0.75–0.93; *P*=0.001; Figure 4).
- The rates of ventilation initiation were similar between the RDV and control groups (14.1% vs 15.7%, respectively; RR, 0.88; 95% CI: 0.77–1; *P*=0.04; Figure 4).
- Safety data were not reported.

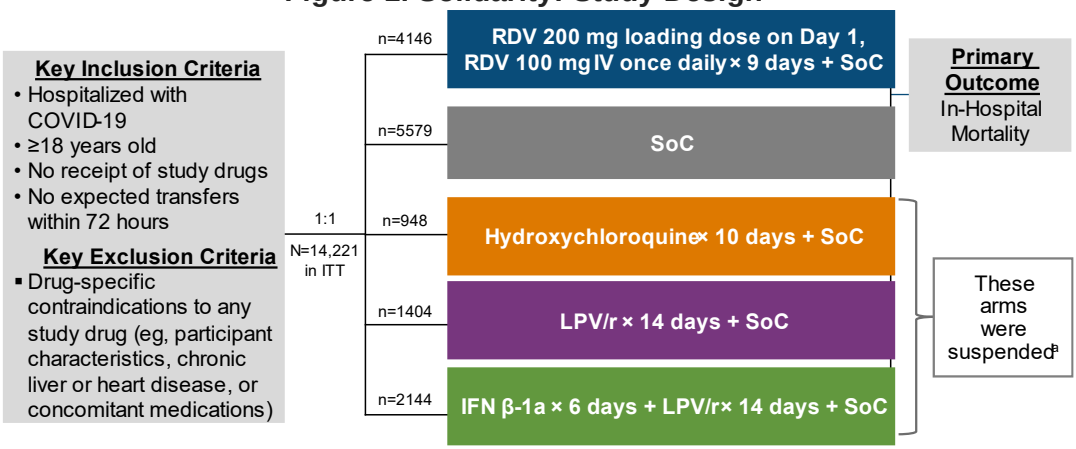
Clinical Data From the Solidarity Study

Study Design and Demographics

The World Health Organization and partners launched Solidarity, an international, randomized, open-label, adaptive, phase 3 clinical trial, to assess potential treatment options for COVID-19. Treatment groups were compared pairwise with control groups for primary endpoint of in-hospital mortality. Prespecified subgroup analyses of mortality were

performed separately for participants with moderate or severe COVID-19; severity was not defined in the protocol, and analyses were conducted for those who required supplemental O_2 or ventilation at the time of randomization.[1]

Figure 1. Solidarity: Study Design[1]



[a]The LPV/r treatment group was discontinued on July 4, 2020, and the hydroxychloroquine treatment group was discontinued on June 19,2020. IFN-β1a was administered with LPV until July 4, 2020, and the treatment group was discontinued on October 16, 2020.

Participants who were enrolled from March 22, 2020, to January 29, 2021, and had follow-up data were included in the ITT analyses (N=14,221). Midway through the treatment course, the rate of treatment adherence in the RDV group was high (95.5%). More than half of all participants (67.1%) in the RDV group also received corticosteroids.[1]

Table 1. Solidarity: Baseline Demographics and Disease Characteristics According to Treatment Group (ITT)[1,2]

Key Demographics and Characteristics, n		RDV (n=4146)	Control (n=4129)
Age	<50 years	1310	1326
	50–69 years	1920	1908
	≥70 years	916	895
Male		2601	2639
Key comorbid conditions (>20% in either group)	Diabetes	1129	1120
	Heart disease	929	935
Days in hospital before study entry	0	888	892
	1	1462	1459
	≥2	1796	1778
Respiratory support	No supplemental O_2	869	861
	Supplemental O_2	2918	2921
	On ventilation	359	347

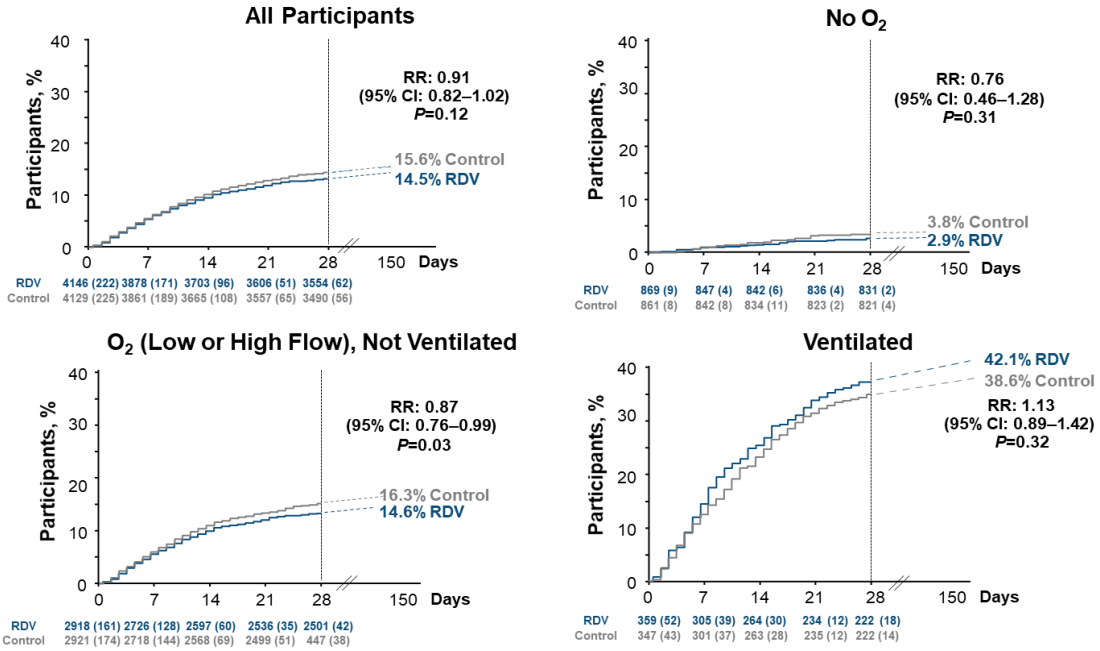
Results[1]

Primary endpoint: mortality

The overall rates of in-hospital mortality at Day 28 were not significantly different between the RDV (14.5% [602/4146]) and control groups (15.6% [643/4129]; RR, 0.91; 95% CI: 0.82–1.02; *P*=0.12; Figure 2). The in-hospital mortality rate included 15 and 11 participants in the RDV and control groups, respectively, who had palliative discharges.

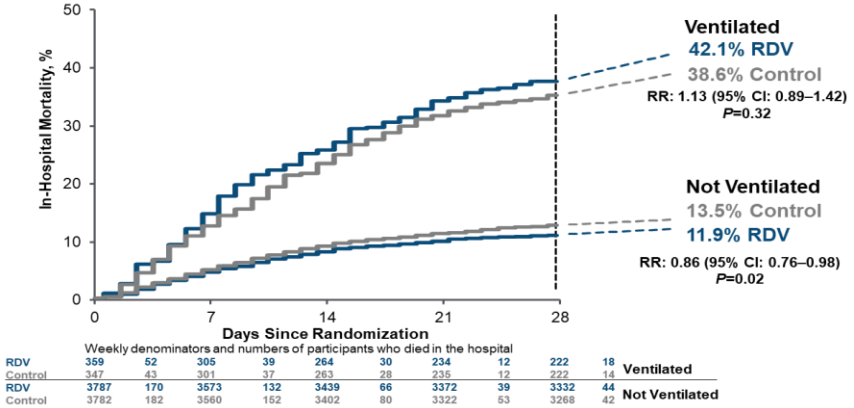
Among those who initially required low- or high-flow O_2 without ventilation, the RDV group had a significantly lower mortality rate than the control group; however, no between-group differences were observed for those who were not on O_2 initially or were ventilated (Figure 2). Among participants who were not ventilated at study entry, fewer participants who received RDV than controls died (11.9% vs 13.5%; *P*=0.02; Figure 3). Fewer participants in the RDV group than in the control group achieved the non-prespecified composite outcome of death or ventilation initiation (19.6% vs 22.5%; *P*=0.001).

Figure 2. Solidarity: Overall In-Hospital Mortality at Day 28 and According to Respiratory Support at Baseline[1]



Note: Kaplan-Meier graphs provided through Day 28 (solid lines), and overall in-hospital mortality rates are provided after Day 28 (dashed lines). Denominators for the Kaplan-Meier graphs include all participants except those who died in the hospital and those who were lost to follow-up. Mortality RRs were standardized for participants' ages and level of respiratory support and incorporated all in-hospital deaths (ie, before or after Day 28). Numbers under each figure represent the weekly denominators and numbers of participants who died in the hospital.

Figure 3. Solidarity: Mortality at Day 28 Among Ventilated and Non-Ventilated Participants[1]



Note: Kaplan-Meier graphs are provided through Day 28 (solid lines), and overall in-hospital mortality rates are provided after Day 28 (dashed lines). The denominators for the Kaplan-Meier graphs include all participants except those who died in the hospital and those who were lost to follow-up. The mortality RRs were standardized for the participants' ages and level of respiratory support and incorporated all in-hospital deaths (ie, before or after Day 28).

Secondary endpoint: time to hospital discharge

Participants who had RDV treatment for ≥7 days were more likely to remain hospitalized on Day 7 than participants in the control group (Table 2). RDV group had a longer hospital stay during the 10-day treatment but similar discharge rates after Day 10 compared to the control group.

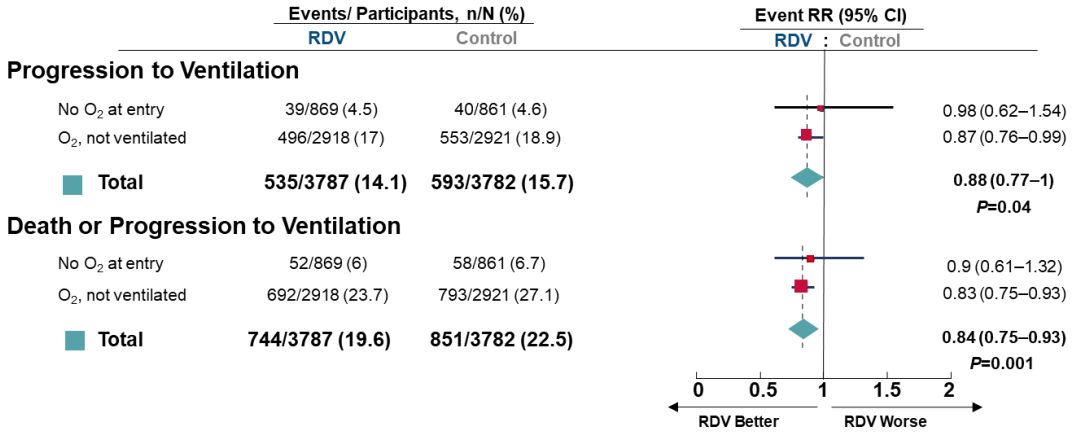
Table 2. Solidarity: Proportions of Participants Who Eventually Discharged Who Were Still Hospitalized at Days 7, 14, and 21[1]

Time Points, %	RDV (n=4146)	Control (n=4129)
Day 7	68.8	62.5
Day 14	25.9	24.7
Day 21	12.4	12.5

Secondary endpoint: initiation of ventilation

Participants who did not require ventilation at baseline and were in the RDV group had a lower rate of ventilation initiation or death than those in the control group (19.6% vs 22.5%, respectively; Figure 4). Ventilation initiation rates were similar between the RDV and control groups (14.1% vs 15.7%; Figure 4).

Figure 4. Solidarity: Progression to Ventilation or Composite Endpoint of Death or Progression to Ventilation After Randomization[1]

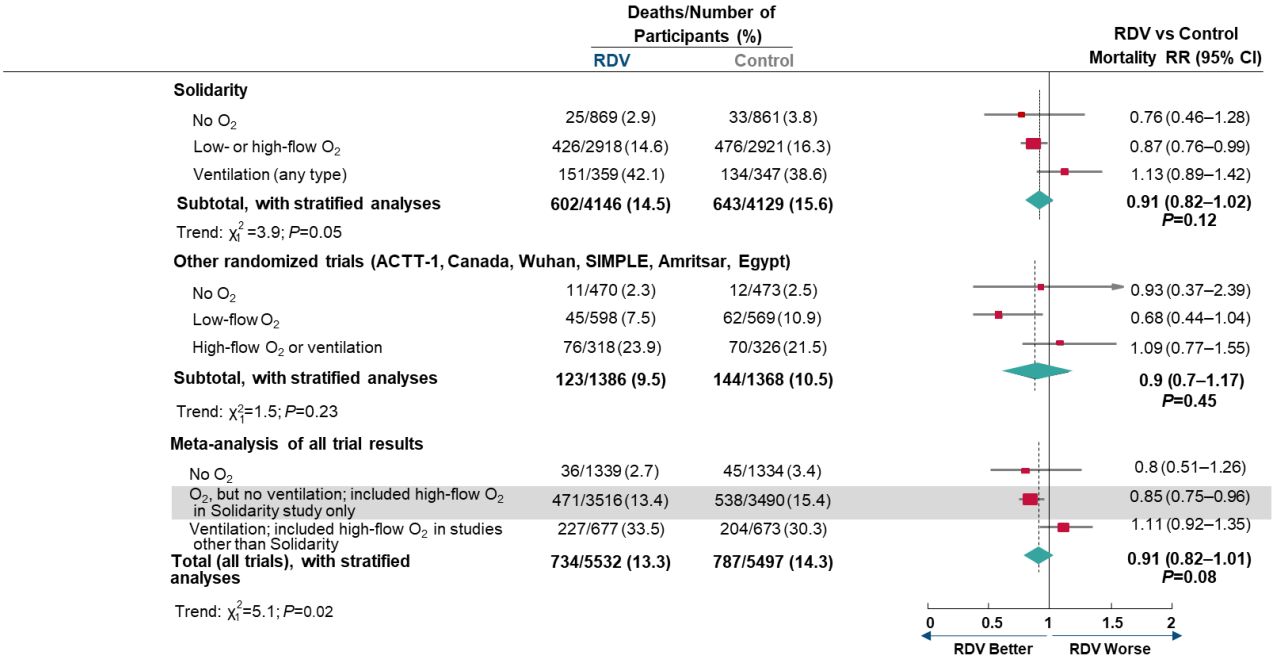


Note: Ventilation includes invasive or non-invasive mechanical ventilation. The use of high- or low-flow O_2 was not recorded separately at entry into the Solidarity study.

Meta-analyses of RDV in studies with hospitalized participants

In meta-analyses of randomized studies that compared RDV with SoC, treatment with RDV was associated with a significant decrease in mortality among participants who required O_2 supplementation but were not ventilated (RR, 0.85; 95% CI: 0.75–0.96; Figure 5); however, the RR for mortality among all participants was not significant (RR, 0.91; 95% CI: 0.82–1.01; *P*=0.08).

Figure 5. Meta-Analyses of the Effect of RDV on Mortality in Solidarity and Other Studies[1]



Note: Ventilation included non-invasive ventilation, and the presence of high- or low-flow O_2 support was not recorded separately at entry into the Solidarity study.

Safety

Safety results were not reported.

References

1. WHO Solidarity Trial Consortium. Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. *The Lancet.* 2022(22).
2. WHO Solidarity Trial Consortium. Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses [Supplementary Appendix]. *Lancet.* 2022.

Abbreviations

IFN=interferon
LPV/r=lopinavir/ritonavir
O_2=oxygen
RDV=remdesivir
RR=rate ratio
SoC=standard of care

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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