Remdesivir has insignificant antiviral effect against SARS-COV-2, but causes serious adverse events

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- In the recommended doses (200 mg on day 1, 100 mg per day after that), Remdesivir (RDV) has only insignificant antiviral effect against SARS-COV-2.
- RDV treatment in accordance with the current recommendations is likely to significantly increase mortality in severe COVID-19 patients.
- Only 3 (three) useful clinical trials have been cited by the FDA in the two EUAs they issued for RDV and by the NIH COVID-19 Treatment Panel in its recommendations to use RDV for COVID-19.
- Only one of the referenced studies claimed clinical benefits of RDV for COVID-19 patients, but it is invalidated by conflicts of interest, misleading reporting of results, suspicious data, and multiple significant changes in the protocol in the middle of the study
- The lack of RDV's antiviral effect for SARS-COV-2 is consistent with the results of its trials for respiratory coronavirus on animals.
- The lack of RDV's antiviral effect for SARS-COV-2 is also consistent with hindsight interpretation of early in vitro trials. RDV and Chloroquine (CQ) have shown similar selective antiviral effects in vitro. However, in vivo, CQ accumulates in lung tissue, while RDV does not. Even with this accumulation, CQ/HCQ is only effective in a synergetic combination with additional medicines, such as Azithromycin (AZ) and/or Zinc.

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Abstract

This paper analyzes all clinical trials referenced by the FDA and the NIH COVID-19 Treatment Panel, in their decisions to issue Emergency Use Authorizations and recommendations for the use of Remdesivir (RDV) for COVID-19 treatment.

Surprisingly, only three comparative clinical trials were cited in four documents issued by the FDA and the NIH, and only one of these studies asserted that RDV treatment was beneficial for COVID-19 patients.

Only one of the three studies - Wang Y. et al. - was conducted without gross conflicts of interest in favor of Gilead Sciences, Inc., the rights owner and manufacturer of RDV. This study found that RDV had no effect in the treatment of COVID-19.

The remaining two studies (Beigel et al., May 22, and Spinner et al., August 21) were marred by gross methodological defects, including changing the primary endpoints in the middle of the study, invalidating their results. Beigel et al. was supposed to be double blind, but it was not. Spinner et al. was not placebo controlled.

Beigel et al. is the only one of these studies that asserted that RDV had clinical benefits in COVID-19 patients. In addition to other defects, it incorrectly reported mortality. The article's text selectively reported the mortality rates after 14 days from the start of treatment, which was lower in the RDV group. However, the results for RDV group deteriorated immediately after that. The mortality rates in severe patients, and only slightly decreased mortality in moderate patients, and severe patients had much higher mortality after RDV treatment than after placebo. The in-depth analysis of this trial's conduct and reporting results indicates a strong bias in favor of the researched product. With a correction for that bias, RDV is likely to increase mortality in the general population of COVID-19 patients, and to sharply increase mortality in severe patients.

Each of the FDA and NIH decisions on RDV only cited one or two useful clinical trials, as follows:

FDA EUA for RDV, May 1:	cited Beigel et al. unpublished data
NIH Panel on RDV, May 12:	cited Beigel et al., Wang Y. et al.
NIH Panel on RDV, July 24:	cited Beigel et al.
FDA EUA for RDV, August 28:	cited Beigel et al., Spinner et al.

The two additional studies cited in the FDA and NIH documents were: Goldman et al. (compared a 5-day RDV treatment course against a 10-day RDV treatment course, with no control group) and Grein et al., (a summary of selected cases from Gilead's early compassionate treatment with RDV, with no control group). Neither of these studies are randomized controlled trials (RTC), nor are they observational studies. They did not compare results of RDV treatment to anything else and could not provide any information in favor of the drug's effectiveness or safety.

The in-vitro and animal studies also show that RDV is not an effective antiviral against SARS-COV-2.

The author declares no conflict of interest.

No funding was provided for this work.

All relevant ethical guidelines have been followed.

Contents

Introduction

On May 1, the FDA issued an emergency use authorization (EUA) for RDV[1] based on unpublished data from two trials: NCT04280705 (later reported by Beigel et al.[2] – conducted by NIAID with participation and/or guidance by Gilead), and NCT04292899 (later reported by Goldman et al.[3] – openly sponsored by Gilead). The EUA did not consider another clinical trial available at that time – Wang Y. et al.[4] (NCT04257656), which found no efficacy of RDV for COVID-19 patients. In September, the FDA expanded its EUA for RDV[5] and cited a third clinical trial: NCT04292730 (reported by Spinner et al.[6] and also sponsored by Gilead Sciences).

NIH's COVID-19 Treatment Panel also recommended RDV as the only antiviral treatment for COVID-19[7] [8], citing two of the above listed trials.

The data to support RDV as a successful treatment for COVID-19 came exclusively from studies sponsored by RDV's manufacturer Gilead Sciences Inc.[9]. Gilead started testing RDV on patients no later than January 25, 2020, as compassionate care[10]. Though Gilead had tens of thousands of potential patients and thousands of doctors throughout the world at its disposal, the published RDV studies reported only a small and cherry-picked selection.

Grein et al., which reported early RDV studies (January 25 - March 7), was heavily criticized in EmCrit[11] for cherry picking of patients and for starting treatment too late, allegedly picking patients that were more likely to improve.

The numbers of COVID-19 patients treated with RDV was much higher than the EmCrit author thought. By March 20, thousands of patients took RDV in the US alone (see raw data in the Supplement of author's *Hydroxychloroquine in COVID-19 Treatment, Actual Usage in the USA*[12]). Gilead selected administering RDV to hospitalized patients, in the post-viral stage of the disease, as the preferred regimen.

In mid-April, a couple of studies hinted that RDV would have no significant antiviral effect against SARS-COV-2. Dr. Sun arrived at the conclusion that RDV is not likely to be effective against SARS-COV-2[13] based on RDV's propensity to evade lung tissue but to accumulate and/or activate in liver. His paper was accepted on April 13 but published only on May 26, with one important change[14]. Wang Y. et al.[4], finding the absence of effectiveness of RDV for COVID-19, was published on April 28.

The FDA's EUA and the NIH COVID-19 Treatment Panel's recommendation for the use of RDV (issued on May 1 and 12 respectively) went contrary to these findings. Both decisions were based on unpublished data from trials either sponsored or influenced by Gilead.

Four months later, independent studies of RDV for COVID-19 are still hard to find. The BMJ maintains a Living Systematic Review of COVID-19 drugs[9]. Updated on September 4, it says: "*Remdesivir was the only intervention where all the data came from randomised controlled trials sponsored by a pharmaceutical company*." It also correctly notes that industry sponsored trials are at risk of publication bias, and positive results require more cautious interpretation. Among 89 references, only three contain the word *remdesivir* in their title (all of them are included here).

Re-Analysis of RDV Studies

This paper re-analyzes the five clinical trial papers that were so heavily relied upon by the FDA and NIH in their decisions to recommend RDV as a COVID-19 treatment.

Only Wang et al. was not marred by conflicts of interest. This trial also showed the absence of statistically significant benefits of RDV for COVID-19, in all measured outcomes. Additionally, the study showed a statistically insignificant increase in mortality for the group treated with RDV.

Clinical Trials

Wang Y. et al., independent, April 29

[4], registered as NCT04257656, sponsored by Capital Medical University, China.

This was a randomized controlled trial, RDV vs placebo, with 237 participants, randomized 2:1. This trial was the only one (of the five trials on the record) pre-registered and without substantial changes in the protocol. The only change was that the number of recruited patients was lower than planned.

Results, comparison between RDV and placebo groups:

- Similar time to clinical improvement in the RDV group and the control group
- Similar 28-day mortality
- Similar "*length of oxygen support, hospital length of stay, days from randomisation to discharge, days from randomisation to death and distribution of six-category scale at day 7, day 14, and day 28*"
- "*Viral load decreased over time similarly in both groups … No differences in viral load were observed when stratified by interval from symptom onset to start of study treatment*"

Mortality was 14% in the RDV group vs. 13% in placebo group. In patients randomized in the first 10 days since onset of symptoms, the RDV group had a shorter time to recovery (18 vs 23 days), although not statistically significant. In patients randomized in the later stages of the disease, the RDV group had a longer time to recovery.

At the time of this trial, a company in China had already prepared to manufacture Remdesivir, with or without a license from Gilead. This eliminates one potential conflict of interest. Eventually, China rejected RDV as a COVID-19 treatment.

Beigel et al., NIAID (& Gilead), May 22

[2], registered as NCT04280705, was conducted in the National Institute of Allergy and Infectious Diseases (NIAID), headed by Dr. Anthony Fauci. It started as "*A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults,*" then became a single drug study. It was reported under the title "*Remdesivir for the Treatment of Covid-19 — Preliminary Report*".

Neither abstract nor the body of the paper contains a conflict of interest disclosure. Only one author reported being an employee of Gilead. But an attached disclosure of potential conflicts of interest reveals five other authors had financial ties to Gilead, including one author who was a member of Gilead's Advisory Board, and two others who received personal fees from Gilead. This fact, and the pattern of obfuscation and cherry picking, like in Grein et al. and Spinner et al., suggests that Gilead was shadow sponsoring this study as well.

The study claimed a faster recovery and lower mortality for those treated with RDV. The latter claim was downplayed by Gilead, but still used.

The average mortality in the RDV group appeared lower than in the control group only on the first measurement date - 14 days after the start of treatment. This was reported. A few days later, the picture nearly reversed. Below are the mortality rates (estimated with Kaplan-Meier estimator) after 24 days from Figure S3. Kaplan–Meier Estimates of Survival by Baseline Ordinal Scale, Supplementary Appendix. The %'s are obtained by taking measures on the chart and are not precise.

	RDV	Placebo
Score 7 (N=272)	22%	15%
Score 6 (N=197)	18%	14%
ALL (N=1059)	12%	13%

Score 7: hospitalized, on invasive mechanical ventilation or ECMO (the most severe subgroup)

Score 6: hospitalized, on high flow oxygen or non-invasive mechanical ventilation.

It shows estimated mortality in the most severe subgroup was 22% for RDV, much worse than 15% for placebo. Taking into consideration the manipulations in the design and conduct of this trial, this apparent result is interpreted here as association of RDV treatment with a sharp increase in mortality in severe patients, no information about RDV in moderate patients, and higher estimated mortality in the total.

Incredibly, the statistical trend reversed again just before the second measurement point, 28 days after the start of the treatment, because 3 patients from the most severe subgroup of the control group died on day 26 after 5 days without deaths. Still, among the most severe patients (scores 6-7), the RDV treated group had lower than the control group odds to survive 28 days from the beginning of the treatment.

There were more than 50 sites in this trial. Such many trial sites, many of which treated only one patient raises suspicions of cherry-picking doctors and/or patients.

The protocol was changed many times during the study. The primary endpoint was changed on April 8 from "*Percentage of subjects reporting each severity rating on an 8-point ordinal scale*" to "*Time to recovery*".

The study was not double blind. Hospitals *"at the European sites and at some non-European sites"* used saline solution instead of matching placebo. The explanation that a $80B company had a placebo shortage for its most important investigational drug cannot be accepted. The trial was intentionally unblinded. Reporting it as double blind is inaccurate.

Many comments[15], published on July 10, pointed out the issues with co-administration of other drugs, and exaggerated estimates of the supposed recovery times decrease. The authors replied to the comments promising to provide the missing information in the final report. As of September 16, the "final report" is still not published.

Two sites with the *Recruiting* status were removed from the study in the May 6 update. This mid-study removal raises suspicions that these sites may have been removed due to undesirable randomization outcomes or unwanted results.

The study did not adequately report the initial conditions of the participants.

These issues invalidate any positive for RDV inferences from this study, even if any appear.

Co-administration of RDV with Hydroxychloroquine (HCQ) was explicitly permitted and admitted.

The paper was published on the same exact day as two other pieces which aimed to discredit HCQ[16], one of which was Mehra et al[17], later retracted due to fraudulent data.

Spinner et al., Gilead, August 21

[6], registered as NCT04292730, was sponsored by Gilead.

The study design kept changing throughout the trial. On April 6, in the middle of the trial, the primary outcome measure was changed from "*Proportion of Participants Discharged by Day 14*" to tricked "*The Odds of Ratio for Improvement on a 7-point Ordinal Scale on Day 11*", invalidating the study.

Even more oddly, the minimum age was changed from 18 to 12 years. Children are hospitalized with COVID-19 extremely rarely. This change in the protocol is a tacit admission that the drug did not work.

The exclusion criteria were also changed during the trial.

Little information about baseline characteristics of compared groups was released. Only stats on four co-existing conditions were released: *Cardiovascular disease* (sic!), *Hypertension*, *Diabetes*, *Asthma*. Not reported PaO_2/FiO_2, blood pressure, heart rate etc.

In admitted violation of the trial's protocol, HCQ/CQ were co-administered with RDV to 11% of the 10-day group and 8% of the 5-days group. AZ was co-administered to 21% and 18%. Moreover, the protocol did not prohibit HCQ/CQ treatment prior to RDV, although the effects of such prior treatment would be long lasting and would continue to have effect in time of the RDV treatment.

HCQ or CQ was administered to 45% of the patients in the control group, because it was a standard of care in the participating hospitals. This is an important footnote.

In the 10-day RDV group, more patients had 5 or less days of RDV treatment than 9-10. The median number of days of treatment was 6.

The table of adverse effects conspicuously lacks information indicating possible liver or kidney damage.

Thus, after running an open-label clinical trial, allowing concomitant HCQ and AZ, changing the primary outcome measures, inclusion and exclusion criteria, the researchers admitted that there was either no difference between RDV and the standard of care, or a difference "*of uncertain clinical importance*".

The deaths were also misrepresented. From eTables 5-6. Clinical Status, Deaths

	RDV	No RDV
Day 14	3 (0.7%)	4 (2.0%)
Day 28	5 (1.3%)	4 (2.0%)

The difference in mortality is not statistically significant, but the actual results are represented by Day 28, while reported results are from Day 14, which looked better for RDV.

Grein et al., Gilead, April 10

[10] was a non-registered study sponsored by Gilead. See the comments in Emcrit[11] about it.

Goldman et al., Gilead, May 27

[3], registered as NCT04292899, was sponsored by Gilead.

Unexpectedly for an experimental drug trial, this trial did not compare RDV with a placebo or another drug but compared a 5-day course of RDV to a 10-day course of RDV.

27% (109/397) of trial participants also received HCQ. When HCQ was co-administered with RDV, the mortality was lower (9% in the HCQ+RDV patients vs 12% in the RDV patients; its Appendix, Table S3. *Baseline Predictors of Time to Clinical Improvement*).

The paper also mentions the concomitant use of Azithromycin but does not provide numbers.

The primary outcome measure was changed on April 6 from *"Proportion of Participants With Normalization of Fever and Oxygen Saturation Through Day 14"* to *"The Odds of Ratio for Improvement on a 7-point Ordinal Scale on Day 14".*

Animal Studies

The effect of a drug depends on the dosage used. An effective antiviral drug must inhibit the virus when administered at doses that do not kill or maim the patient. RDV seems to work against respiratory coronaviruses at toxic doses.

The NIH Panel recommendation for RDV mentioned Williamson et al.[18], a study of RDV against SARS-COV-2 in rhesus macaques. Indeed, the macaques, treated with large RDV doses, had lower lung viral levels and less lung damage. However, the Panel did not mention that the safety

of these doses was not checked, and the macaques were euthanized 6 days after the beginning of treatment.

Williamson et al. also stressed that the viral dynamic in macaques was different from humans. Even untreated macaques did not get severe sickness from SARS-COV-2. The viral loads decreased from the first day in both treated and untreated macaques.

The effectiveness of RDV against SARS-COV-2 in macaques were slightly below that against MERS in macaques[19], consistent with other evidence of low antiviral activity of RDV against SARS-COV-2.

In Vitro

Wang M. et al.[20] demonstrated that RDV & CQ had similar effectiveness in vitro. In vivo, CQ and HCQ work because their metabolites accumulate in the lungs' tissue. RDV's derivatives do not accumulate in lungs. Additionally, the effectiveness of HCQ alone against SARS-COV-2 is only moderate. HCQ is highly effective only when combined with AZ and/or Zinc.

Discussion and Remarks

All studies show that RDV in recommended doses (100 mg per day, 200 mg on the first day), is not effective against SARS-COV-2. The summary of the studies:

- Only Gilead sponsored studies (inclusive of Beigel et al., which appears conducted through NIAID rather than by NIAID) claim positive results of RDV in COVID-19 patients
- None of the Gilead's sponsored studies were double blind, or with adherence to the pre-registered protocol.
- Only Beigel et al. makes a firm claim of RDV benefits in comparison to a placebo. These claims are contradicted by its own raw data and invalidated by multiple violations of the protocol and inaccurate information about the role of the drug manufacturer in the study.

The FDA's EUA, from May 1, recommended the use of RDV in severe COVID-19 patients. Based on the information that was available at that time, this was the worst use of RDV, potentially leading to 50% higher mortality in severe patients treated with RDV.

Metabolites of both RDV (GS-441524 triphosphate) and CQ/HCQ (4-aminoquinolines), in concentrations that are safe to in vitro cell culture, can inhibit SARS-COV-2, but metabolites of

HCQ accumulate in the lung tissues[21] (and retina, which retains only very small amount of them) and inhibit the virus, while metabolites of RDV accumulate and/or activate in liver and kidneys[22].

HCQ does not decrease putative antiviral effectiveness of RDV[23], as was alleged by the FDA based on communication from Gilead. Quite the opposite, some clinical studies have shown a synergistic effectiveness of CQ/HCQ + RDV combination[24] against SARS-COV-2. Results of Goldman et al. are consistent with this conclusion.

Spinner et al. reveal that in March - April, Hydroxychloroquine was part of the standard of care in hospitals half of their patients were treated. Since then, the antiviral effectiveness of HCQ with Azithromycin and/or Zinc has been demonstrated in dozens of studies[25].

RDV damages the liver[26] and kidneys[22].

Yanis Roussel and Didier Raoult[27] have shown that support for RDV vs HCQ in France matches financial incentives from Gilead.

In 2019, the FDA refused to approve RDV for treatment of cats against an unrelated coronavirus disease[28].

The contradictory aspect of the FDA authorization for treatment of severe (i.e., late stage) patients with a putative antiviral, which is supposed to be given early in the viral phase of a disease, was noticed by doctors[29].

Conclusion

Remdesivir is not an effective antiviral against SARS-COV-2. Remdesivir shows no benefits in COVID-19 and increases mortality among severe patients.

No Conflict of Interest

The author declares no conflict of interest.

No funding was provided for this work.

All relevant ethical guidelines have been followed.

References

1. Wayback Machine. Published May 2, 2020. Accessed September 17, 2020. https://web.archive.org/web/20200502210307/https://www.fda.gov/media/137564/download

2. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 — Preliminary Report. *N Engl J Med*. Published online May 22, 2020. doi:10.1056/NEJMoa2007764

3. Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. *N Engl J Med*. Published online May 27, 2020. doi:10.1056/NEJMoa2015301

4. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *The Lancet*. 2020;395(10236):1569-1578. doi:10.1016/S0140-6736(20)31022-9

5. The FDA. Letter of Authorization, August 28, 2020. Published August 28, 2020. Accessed September 17, 2020. https://www.fda.gov/media/137564/download

6. Spinner CD, Gottlieb RL, Criner GJ, et al. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. *JAMA*. Published online August 21, 2020. doi:10.1001/jama.2020.16349

7. The NIH COVID-19 Treatment Panel. Remdesivir | Coronavirus Disease COVID-19. Published May 1, 2020. Accessed September 17, 2020. https://web.archive.org/web/20200512220006/https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/remdesivir/

8. The NIH COVID-19 Treatment Panel. Remdesivir | Coronavirus Disease COVID-19. Published July 24, 2020. Accessed September 17, 2020. https://web.archive.org/web/20200803141343/https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/remdesivir/

9. Siemieniuk RA, Bartoszko JJ, Ge L, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ*. 2020;370:m2980. doi:10.1136/bmj.m2980

10. Grein J, Ohmagari N, Shin D, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. *N Engl J Med*. 2020;382(24):2327-2336. doi:10.1056/NEJMoa2007016

11. Farkas J. Eleven reasons the NEJM paper on remdesivir reveals nothing. EMCrit Project. Published April 11, 2020. Accessed September 17, 2020.

https://emcrit.org/pulmcrit/pulmcrit-eleven-reasons-the-nejm-paper-on-remdesivir-reveals-nothing/

12. Hydroxychloroquine in COVID-19 Treatment, Actual Usage in the USA. Watts Up With That? Published August 24, 2020. Accessed September 17, 2020. https://wattsupwiththat.com/2020/08/24/hydroxychloroquine-in-covid-19-treatment-actual-usage-in-the-usa/

13. Sun D. Remdesivir for Treatment of COVID-19: Combination of Pulmonary and IV Administration May Offer Aditional Benefit. *The AAPS Journal*. 2020;22(4):77. doi:10.1208/s12248-020-00459-8

14. Goldstein L. Fauci Knew that Remdesivir Ineffective. Accessed September 17, 2020. https://defyccc.com/fauci-knew-remdisivir-ineffective/

15. Correpondence regarding: Remdesivir for the Treatment of Covid-19 — Preliminary Report. *N Engl J Med*. 2020;383(10):992-994. doi:10.1056/NEJMc2022236

16. Goldstein L. The Lancet Doubles Down on anti-HCQ Fraud. Accessed September 17, 2020. https://defyccc.com/the-lancet-doubles-down-on-anti-hcq-fraud/

17. Mehra, et al. RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis - The Lancet. Accessed August 6, 2020. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31180-6/fulltext

18. Williamson BN, Feldmann F, Schwarz B, et al. Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2. *Nature*. 2020;585(7824):273-276. doi:10.1038/s41586-020-2423-5

19. de Wit E, Feldmann F, Cronin J, et al. Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. *Proc Natl Acad Sci USA*. 2020;117(12):6771. doi:10.1073/pnas.1922083117

20. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Research*. 2020;30(3):269-271. doi:10.1038/s41422-020-0282-0

21. Browning DJ. Pharmacology of Chloroquine and Hydroxychloroquine. In: Browning DJ, ed. *Hydroxychloroquine and Chloroquine Retinopathy*. Springer New York; 2014:35-63. doi:10.1007/978-1-4939-0597-3_2

22. Yan VC, Muller FL. Advantages of the Parent Nucleoside GS-441524 over Remdesivir for Covid-19 Treatment. *ACS Med Chem Lett*. 2020;11(7):1361-1366. doi:10.1021/acsmedchemlett.0c00316

23. Goldstein L. The Myth that HCQ Interferes with RDV. Accessed September 17, 2020. https://defyccc.com/myth-hcq-interferes-with-rdv/

24. Scavone C, Brusco S, Bertini M, et al. Current pharmacological treatments for COVID-19: What's next? *British Journal of Pharmacology*. 2020;n/a(n/a). doi:10.1111/bph.15072

25. @CovidAnalysis. COVID-19 Treatment Analysis. Accessed September 17, 2020. https://c19study.com/

26. Zampino R, Mele F, Florio LL, et al. Liver injury in remdesivir-treated COVID-19 patients. *Hepatol Int*. Published online July 28, 2020. doi:10.1007/s12072-020-10077-3

27. Roussel Y, Raoult D. Influence of conflicts of interest on public positions in the COVID-19 era, the case of Gilead Sciences. *New Microbes and New Infections*. Published online June 6, 2020:100710. doi:10.1016/j.nmni.2020.100710

28. Mokobi F. Remdesivir- Mechanism of Action, Uses, Synthesis & COVID-19. Microbe Notes. Published April 19, 2020. Accessed September 17, 2020. https://microbenotes.com/remdesivir/

29. COVID-19 Press Releases. Sermo. Accessed September 17, 2020. https://www.sermo.com/covid-19-press-releases/