# Remdesivir is least likely to be effective for safe treatment of COVID-19: A pharmacovigilant point of view

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**Abstract**

This manuscript has been published on the 29 th of May 2020 by the honorable BMJ as a rapid response to a related article. However since a DOI has not been assigned and two subsequent manuscripts have cited it, I'm preprinting a copy wishing it might reach all the interested colleagues and researchers in an easier way.

This manuscript has been published on the 29$^{\text{th}}$ of May 2020 by the honorable BMJ as a rapid response to a related article. However since a DOI has not been assigned and two subsequent manuscripts have cited it[1,2], I'm preprinting a copy wishing it might reach all the interested colleagues and researchers in an easier way.

Dear Editor,

I've read with much interest a recent article published at your honorable journal discussing the decision made by NIH to select some hospitalized COVID-19 patients to test the potential of the investigational drug remdesivir and the author was very concerned that a previous trial has never been finished and it's becoming hard to recruit patients to be tested for this drug[3] and I'd like to try to answer his concern from a pharmacovigilant point of view.

The results published in the Lancet by Wang and colleagues, have showed no statistically significant COVID-19 benefits for remdesivir treatment beyond those of standard of care treatment but unfortunately, the authors have recommended "future studies of remdesivir, including earlier treatment in patients with COVID-19 and higher-dose regimens or in combination with other antivirals or SARS-CoV-2 neutralising antibodies in those with severe COVID-19 are needed to better understand its potential effectiveness"[4]. Wang and colleagues have clearly stated that the primary endpoint of time to clinical improvement was not significantly different between groups and that all-cause mortality at day 28 was 14% in the remdesivir arm as compared to 13% in the placebo for patients with late use of remdesivir. However, they reported a numerically higher mortality, but also non-significant, in the placebo group if remdesivir used early during COVID-19 and perhaps this might have been one of the reasons for their positive recommendation that led NIH to unfortunately continue trying to recruit more selected patients to continue the failing trials.

Similarly, I also disagree with any suggested clinical significance of their observation that those receiving remdesivir had a numerically faster time to clinical improvement than those receiving placebo. This non-significant numerical interpretation of clinical results related to this investigational, experimental and potentially hazardous remdesivir should be considered irrelevant from my pharmacovigilant point of view.

Noteworthy, it's crucial to notice that they've also reported that remdesivir produced adverse events leading to its stoppage in 18 (12%) patients versus four (5%) patients who stopped placebo early, and I suggest that these results are the most important reported numerical, as well as significant findings and I recommend

them to be considered very carefully looking for a deeper analysis of these adverse effects that might have helped to encourage the investigators to prematurely stop remdesivir clinical trial. The adverse events have not only included minor gastrointestinal symptoms (anorexia, nausea, and vomiting), but also aminotransferase or bilirubin increases, and most importantly worsened cardiopulmonary status as stated in Wang and colleagues published manuscript. From a pharmacovigilant point of view, I recommend all colleagues working on each undergoing remdesivir clinical trial to fully investigate the cardiopulmonary adverse effects as it might eventually resemble that of hydroxychloroquine that is being revealed both ineffective and potentially hazardous [5] and started to be banned by some countries for further use for COVID-19[6].

Unfortunately, on the same day Wang and colleagues published their results, another numerical misinterpretation, as I suggest, of data has been made by the National Institute of Allergy and Infectious Diseases (NIAID), an NIH affiliated entity which has reported the median time to recovery was 11 days for COVID-19 patients treated with remdesivir compared with 15 days for those who received placebo and it was surprisingly officially declared as a 31% faster time to recovery[7]. I consider this and similar claims as totally misleading and I believe that it should be only interpreted as 4 days difference compared to placebo, this doesn't by any means deserve to be focused on through a press release, nor justified as reason for early termination of the study, taking also into consideration that even in this study, no significant difference in remdesivir mortality rate compared to placebo was observed and I'm waiting for the full results to be published looking for other confounding factors that might be also present.

Interestingly, I would like to refer all my colleagues to read the full press release statement wisely made by remdesivir manufacturer's Gilead on the same day these results have been misinterpreted by the media as well as by stock markets that soared its shares, I'm only quoting short excerpts:

"Remdesivir is not yet licensed or approved anywhere globally and has not yet been demonstrated to be safe or effective for the treatment of COVID-19. Further, it is possible that Gilead may make a strategic decision to discontinue development of remdesivir or that FDA and other regulatory authorities may not approve remdesivir, and any marketing approvals, if granted, may have significant limitations on its use. As a result, remdesivir may never be successfully commercialized"[8] to be noted that Gilead is sponsoring multiple clinical trials all over the world for its remdesivir potential for COVID-19[9] and I suggest it knows better than NIAID about its efficacy and safety.

Finally, the main bulk of this manuscript was submitted on the first of May to The Lancet and on the 11th of May, NIH has declared that it has stopped its big remdesivir trial and so I wish to thank all the honorable scientists who fought with honor to make this decision appear[10], to be noted that I've received the formal "The Lancet" rejection without peer-review comments on the 21st of May.

Conflict of interests

None

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None

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