OPEN ACCESS Freely available online

Journal of Clinical Trials

Commentary

The Sinking of Clinical Trials! How Wrong done by a Virus could have Undermine Rigor and Compromises Response to Emergency

F. Tremolieres*

Department of Internal medicine-Infectious Disease, François-Quesnay Hospital, 78200 Mantes-la-Jolie, France

STUDY DESCRIPTION

During the first six months of the Covid-19 outbreak, nearly 2,000 clinical trials involving drugs were registered.

Who has ever seen in the past, in so short time, such a rush to drug trials for the same disease?

Who has ever seen such a prompt media broadcast of any trial, whether it shows any preliminary results, positive or not?

Worse! Any announcement of a product that is supposed to do something is immediately promoted, and we push for trials to start "subito" as our Italian friends say. We remember what happened with nicotine, chlorpromazine, ivermectin and so many others, not forgetting various Chinese plants.

Research has never seemed to be so fast, with an incredible reduction in the time taken by sponsors to develop their projects, agencies and ethics committees to validate the authorization of trials, and by an evaluation that has already been published before being validated.

What usually takes months was done in 15 days, often seven, and even in 48 hours.

The public's legitimate expectation for effective treatments cannot justify inappropriate methods, botched trials, under-staffed studies, and let alone a communication eager for exclusivity.

Did the global panic justify engaging in such a mess of clinical trials that were too small and of questionable methodological quality?

The article published at the beginning of July in the journal MMI [1] highlights that after six months this rush of trials and disorganized announcements resulted in a TOTAL FAILURE - no drug has identified a positive, relevant, significant effect that would allow a validated recommendation for use to be made.

Two main examples are cited here

That of hydroxychloroquine

When, on 25 February 2020, Professor Didier Raoult announced in a video broadcast around the world "that respiratory infection (of the coronavirus) is the easiest to treat" and that his expertise made it possible to announce that chloroquine was the undisputed drug; in addition to the incongruity of such a communication, a controversy arose which is not yet over, although the initial assertion has been largely denied.

In the following weeks, the Marseille team will manifest itself through a series of statements and several publications of the IHU - Mediterranean [2-6]. The effectiveness of hydroxychloroquine, which has been discussed by observational studies without any direct comparison, remains obvious and unquestionable for their authors.

The controversy was revived when the journal The Lancet published results on 22 May that largely invalidated the stated efficacy [7]. But disaster! A few days later this study is itself ruined by its own investigators, and this major Britannic journal is forced to retract, and even to withdraw the article. In the media they talk about Lancet-gate!!!

Then the saga continues on June 3, a true, randomized trial [8] was published in the NEJM, showing no effect in prophylaxis. Only one trial!

The story accelerated again on June 5, when the chloroquine arm of the English "Recovery" trial was suspended. "We concluded that hydroxychloroquine has no beneficial effect on patients hospitalized with Covid-19," declared its promoters.

On June 9, the controversy persists, and it was not the Franco-European "Discovery" trial that was going to be able to advance knowledge. This trial raises too many questions.

To date, it is accepted that chloroquine has not shown any effect; but what a mess. So many people remain certain that the effectiveness of the product has been covered up; evaluation is done by survey, science is replaced by faith: "I believe, I know!"

The situation of the remdesivir trials is not much brighter.

Correspondence to: F. Tremolieres, Department of Internal medicine-Infectious Disease, Francois-Quesnay Hospital, 78200 Mantes-la-Jolie, France, E-mail: ftremo91@gmail.com

Received date: August 17, 2020; **Accepted date:** August 29, 2020; **Published date:** September 07, 2020

Citation: Tremolieres F (2020) The Sinking of Clinical Trials! How Wrong done by a Virus could have Undermine Rigor and Compromises Response to Emergency. J Clin Trials. S3:002.

While around 30 trials are underway, but no results have been published, efficacy data has been leaked. At the end of March, at the request of Estonia, Greece, the Netherlands and Romania, the EMA began reviewing an authorization dossier for remdesivir. The CHMP opinion is dated April 3, 2020 and authorizes this product for compassionate use.

The FDA will be slower but just as surprising. It will wait until May 1 to give "an emergency-use authorization". But extreme publicity was given to this decision when two days earlier, on April 29, the news was announced directly from the White House by the President of the United States himself! "I am pleased to report that Gilead has received emergency use approval from the FDA for remdesivir".

We see that drug approvals are now being given from the Oval Office of the White House. Politics and conflicts of interest have taken over science!

One could imagine such a procedure if a MIRACULOUS treatment had just been discovered.

Remdesivir may not be without effect, but to speak of a miracle would be extravagant! Two months later it is registered for varying use in different countries. Its usefulness for the treatment of severe forms of Covid-19 remains to be established. In particular there is no mortality data in this single trial [9]. Normally this drug should never have received Marketing Authorization with a single clinical trial and so little data for minimal efficacy possible.

Many other trials have involved other drugs; most antiviral drugs have not shown efficacy, they are not cited here. But we must remind those who seek that the development of antivirals has a generally very complicated, with long history for development, as we have seen with acyclovir and its derivatives, and treatments for AIDS, hepatitis, and influenza.

It should be remembered that the organization of clinical trials should always be done by taking one's time, by working, by setting up valid multicentre trials; they require large resources, will mobilize large teams, and their financing is not simple.

For the actual period, the race for a miracle is responsible for the sinking.

REFERENCES

1. The wreck of "clinical trials"! Or how the misdeeds of a virus could have undermined rigor and compromised the emergency response. Rise and fall of clinical trials! How wrong done by a virus could have undermine rigor and compromises response to emergency F. Trémolières. Med Mal Infect. 2020.
2. Gautret P, Lagier JC, Parola P, Meddeb L, Mailhe M, Doudier B, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: Results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020;20:105949.
3. Gautret P, Lagier JC, Parola P, Meddeb L, Sevestre J, Mailhe M, et al. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study. Travel Med Infect Dis. 2020;11:101663.
4. Million M, Lagier JC, Gautret P, Colson P, Fournier PE, Amrane S, et al. Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France. Travel Med Infect Dis. 2020;5:101738.
5. Lagier JC, Million M, Gautret P, Colson P, Cortaredona S, Giraud-Gatineau A, et al. Outcomes of 3,737 COVID-19 patients treated with hydroxychloroquine/azithromycin and other regimens in Marseille, France: A retrospective analysis. Travel Med Infect Dis. 2020;36:101791.
6. Million M, Gautret P, Colson P, Roussel Y, Dubourg G, Chabriere E, et al. Clinical Efficacy of Chloroquine derivatives in COVID-19 Infection: Comparative meta-analysis between the Big data and the real world. New Microbes and New infect. 2020;6:100709.
7. Boulware DR, Pullen MF, Bangdiwala AS, Pastick KA, Lofgren SM, Okafor EC, et al. A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19 D. N Engl J Med. 2020.
8. Mehra MR, Desai SS, Ruschitzka F, Patel AN. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: A multinational registry analysis. Lancet. 2020.
9. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the Treatment of Covid-19 Preliminary Report. N Engl J Med. 2020.