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## Merck Ignores Molnupiravir's Cytotoxicity

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Merck has just applied to the FDA for an emergency use authorization of Molnupiravir for early treatment of COVID-19. Molnupiravir is a mutagenic nucleotide analogue. It increases the rate of mutations in the coronavirus' RNA and in human DNA.

The application is based on alleged interim results of an unfinished trial, where this drug was given to 385 patients in 173 sites all over the world, and the patients were then observed for 29 days since recruitment and randomization.

Molnupiravir is mutagenic and toxic for human cells. Merck and Ridgeback Biotherapeutics have flatly denied this and proceeded with human trials. The consequences of Molnupiravir's DNA mutagenesis, such as cancer or birth defects, take months or years to develop. The 24 days of patient observation after 5 days treatment is obviously not enough to detect anything.

The broad use of [Molnupiravir is a global catastrophic risk](#) because the increased rate of coronavirus mutations is likely to create more dangerous variants.

All Molnupiravir trials were conducted by Merck or its partners. No results have been published in peer reviewed journals. Nevertheless, Dr. Fauci gave it a nod of approval. The US government has already purchased 1.7 million "treatment courses" from Merck, and it is on the course to manufacture and ship 10 million of them by the end of 2021. The relevant parties act as if the EUA approval is just a formality and are proceeding as if it were already granted.

### Introduction

Merck acquired all rights for Molnupiravir, which was co-developed by Ridgeback Biotherapeutics LP and DRIVE LLC, owned by Emory University <sup>[1]</sup>, so all of their Molnupiravir-related work is referred here as Merck's. Emory University is located next to the national CDC HQ in Atlanta, GA.

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<sup>1</sup> [ah@defyccc.com](mailto:ah@defyccc.com)

<sup>2</sup> <https://trialsitenews.com/merck-ignores-molnupiravirs-cytotoxicity/> (publication)  
<https://defyccc.com/merck-hid-molnupiravir-cytotoxicity-and-genotoxicity/> (updates)

## Cytotoxicity

Molnupiravir is a mutagenic <sup>[2] [3] [4] [5] [6]</sup> nucleotide analogue, and its potential cytotoxicity and genotoxicity are not in doubt <sup>[7]</sup>. Its use for some categories of patients could be justified if benefits were exceeding harm and risk. Instead, Merck elected to deny existence of these risks.

Molnupiravir's metabolites cause mutations in human DNA <sup>[4]</sup>, just like they do in viral RNA. This is not in question. If the rate of mutations at therapeutic doses were sufficiently low, Merck should have shown that. Merck's researchers dismissed this danger by alleging that they had conducted tests showing an absence of cytotoxicity <sup>[8]</sup>, without showing any data. Their response was rebutted <sup>[7] [9]</sup> and laughed at by other scientists <sup>[9]</sup>.

The therapeutic dosage -- 800 mg, twice daily, for 5 days -- is at the upper limit of the investigated range 50 - 800 mg <sup>[10]</sup>, suggesting it is higher than what was initially expected.

Molnupiravir was initially developed to treat Equine Encephalitis virus diseases, and its most valuable property was its ability to cross brain-body barrier and achieve high concentration in the brain and very high concentrations in spleen <sup>[11]</sup>. Its concentration in the spleen is higher than in lungs <sup>[3]</sup>.

<sup>[3]</sup> showed that meaningful inhibition of SARS-COV-2 without cytotoxicity is impossible in Vero cells (Fig. 1B). The data for human epithelial cells is inconsistent but does suggest cytotoxicity (Supplementary Materials, the data for Fig. S1).

## More Mercky Business

<sup>[9]</sup> Merck researchers admitted to the necessity of in-vivo mutagenicity studies for this drug before proceeding to human trials. They therefore claimed that such studies (*Pig-a* and the *Big Blue*<sup>®</sup> (*cII Locus*)) have been conducted and that no danger of mutagenicity was found even at higher doses <sup>[12]</sup>. This is highly unlikely. Moreover, other scientists argued that these studies had significant limitations and do not allow Merck to make such claims <sup>[9]</sup>. To make matters worse, Merck failed to publish any data from these studies, making it impossible to peer review or replicate them. This raises suspicions not only about the toxicity of Molnupiravir, but also about Merck's conduct before and during clinical trials.

No data about concentrations and effects of Molnupiravir's metabolites in the most vulnerable tissues, such as bone marrow, can be found.

## Dubious Results from Animal Trials

Animal trials also failed to provide evidence of Molnupiravir's effectiveness, at the manufacturer's recommended dose - 800 mg (equivalent of 10 mg/kg or **370 mg/m<sup>2</sup>**) twice daily. The mass of the drug per body area of the human or animal is the preferred quick approximation for comparison between human and animal doses <sup>[13]</sup>.

Human lung mice <sup>[3]</sup> were treated for SARS-COV-2 infection with Molnupiravir at doses 50, 150, and 500 mg/kg twice daily. Symptomatic improvement was observed at 500 mg/kg (**1,500 mg/m<sup>2</sup>**) but not at 150 mg/kg (**450 mg/m<sup>2</sup>**). Explanations have been put forward, but this trial looks negative for Molnupiravir.

Syrian hamsters <sup>[14]</sup>, likely the best animal model for SARS-COV-2 ,were treated for COVID-19 with Molnupiravir at doses 200 mg/kg (**1,000 mg/m<sup>2</sup>**) twice daily successfully. Treatment started with pre-exposure prophylaxis and continued for 4 days. Because of the high dose and the pre-exposure use, this trial does not provide positive for Molnupiravir evidence.

Ferrets <sup>[15]</sup> were treated for COVID-19 with Molnupiravir at doses starting with 5 mg/kg (**35 mg/m<sup>2</sup>**) twice daily successfully, but ferrets cannot develop large viral loads or severe disease. This trial does not provide positive for Molnupiravir evidence, either.

The failure of the drug in animal trials is reminiscent of Gilead's Remdesivir.

### The "Phase 3" Trial

Merck applied for Molnupiravir's EUA based on Part 2 of the clinical trial registered as NCT04575597 <sup>[16]</sup>.

In this trial, Merck gave patients in the treatment group 800 mg x 2/day x 5 days. After observing 775 participants (including 385 in the treatment group) for 24 (= 29-5) days after that, Merck published a press release <sup>[17]</sup> claiming that the trial was successful.

It is not true. A formally registered clinical trial should be conducted according to the plan until the end to provide statistically valid results. It was registered to enroll, randomize, and observe 1550 participants, and Merck had to spend another month to do that. Its October 1 press-release stated that the recruitment was more than 90% complete at the time it was stopped, between September 5 and September 30. After 20 months of the pandemic, making decisions one month before completion of the single Phase 3 trial looks fishy.

If we combine this trial with a few dozen patients who received the same dose of Molnupiravir in other trials, there are less than 500 patients in total, who were treated with this drug and observed for 29 days. Should a drug be authorized for tens of millions of people, based on a trial involving less than 500 patients?

This trial was conducted in 173 sites all over the world. Such a wide range of sites cannot be properly controlled. This trial looks like a reality show, in which the organizers control the outcome. Gilead used a similar methodology to push Remdesivir, with deadly results. Merck's Molnupiravir gambit is even more dangerous, because it can be administered to millions, with catastrophic global risks <sup>[18]</sup>.

Finally, no study plan or protocol of the trial has been published and of course, no results. The only morsels of information to be found on this trial comes from Merck's press release and ClinicalTrials.gov <sup>[16]</sup>, which does not contain even the protocol ID.

Two Indian companies also started clinical trials for Molnupiravir but decided to stop, apparently because of futility <sup>[19]</sup>, but another Indian company Hetero applied for an EUA in India.

## Conflicts of Interest and Hidden Motives

The conflict of interest is unusually high. Merck has been manufacturing Molnupiravir at risk<sup>[17]</sup>. Payment is conditional on EUA:

*“In anticipation of the results from MOVE-OUT, Merck has been producing molnupiravir at risk. Merck expects to produce 10 million courses of treatment by the end of 2021, with more doses expected to be produced in 2022.”*

The US and other governments, who ordered Molnupiravir<sup>[20]</sup>, carry an even bigger risk. They have created expectations that would go unfulfilled if Molnupiravir is properly rejected. Such an evident alignment of interests between government bureaucracies and Merck is very dangerous and requires extreme scrutiny.

## Conclusion

With the current limited information about Molnupiravir, one might compare its effects, at the “therapeutic dosage”, to a medium dose of radiation. There might be acute sickness, temporary immune-suppression, and long-term consequences including cancer and birth defects. The specific dosage may have been selected to be just below the threshold of acute sickness. We will not know until the results are published.

## Catastrophic Risk

Molnupiravir increases mutagenesis of SARS-COV-2 potentially leading to the rise of a highly resistant and virulent variant<sup>[18]</sup>. A small trial by Merck<sup>[21]</sup> has shown nearly doubling coronavirus nucleotides mutations on day 5, probably at the low 200 mg dose.

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