Peg-interferon Lambda Single Dose Treatment for COVID-19: A Call to Avoid another Hydroxychloroquine Fiasco.

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Abstract

In this perspective, I counter-argue a claim that was recently made that a single dose of Peg-interferon lambda can significantly lower incidence of COVID-19 hospitalizations or emergency department visits. Some major flaws in a recently published article that suggested this benefit are discussed while asking the global authorities to learn from the prior mistakes and to be of utmost caution when considering its final decision regarding adoption of a single dose of Peg-interferon lambda to manage COVID-19.

Keywords

COVID-19, Peg-interferon lambda, Eiger BioPharmaceuticals.

Key summary points

Single dose of Peg- interferon lambda is unlikely to benefit COVID-19 patients, yet heavily advertised globally.

Kelleni's protocol could have ended COVID-19 pandemic since April 2020, yet heavily censored by stakeholders in the western media; it's too economic using generic drugs.

Trials supported by big pharmaceutical companies especially in the developing countries should be cautiously interpreted.

The decisions of the American FDA should never be taken for granted especially at the times of pandemics.

Since the start of COVID-19 pandemic, one of the worst calamities in human history, and for over three years, most people all over the developed world felt despair while suffering from many pitfalls regarding its unwise policies and pharmacotherapy, which is mostly controlled by the decisions of the American FDA and CDC [1]. Over 6.8 million people have lost their life and it's almost globally agreed that this number is underestimated though in less dramatic manner as the numbers of the real infections that weren't reported or shown in the CDC estimates and the losses and underestimation are continuing [1, 2].

Recently, the world was flooded with a piece of news, translated in all written languages including my mother tongue; Arabic, in advertisement of the results of a Brazilian (98.5% of the participants) clinical trial, which is supported by the American Eiger BioPharmaceuticals that since 2016 has collaborated with the American Bristol Meyers Squibb and its subsidiary ZymoGenetics to develop the investigational pegylated interferon lambda 1a, also known as PEG-IL-29, claiming that one dose injection of peg-interferon Lambda is "the best treatment of COVID-19" and "almost all patients should receive it soonest". This has occured after a paper was peer-reviewed and published at the American NEJM [3]. Meanwhile, two correspondences, published at highly reputable and professional journals, describing how a real-life Egyptian protocol using generic nitazxoanide, as an integral component, is continuing throughout the pandemic to safely and effectively manage COVID-19, RSV, influenza and norovirus infections [4, 5] together with a unique call to learn from and follow Africa and abort all the remaining COVID restrictions and/or mandates [1, 6], were censored by stakeholders controlling both the western media and the western drug and health regulatory authorities deciding how to manage COVID-19 for reasons which are most likely to lie beyond the scope of medicine and science; Kelleni's protocol is too economic using generic drugs and could have wasted billions of dollars that were gained by companies promoting remdesivir, Paxlovid, monoclonal antibodies, N95 masks and surely vaccines[7-9].

The aforementioned clinical Brazilian trial claimed a significantly lower incidence of COVID-19 hospitalizations or emergency department visits among those who received a single dose of pegylated interferon lambda compared to placebo [3]. However, according to my experience regarding the use of interferons in COVID-19 [10-13], I claim that this trial is highly unlikely to achieve the published outcomes, to be noted that my current counterargument, containing three

major points, was declined on 15 February 2023, without any editorial comment, to be published at NEJM (ID 23-01880) and this reminds me of their previous comment-less denial to publish my criticism to the RECOVERY results regarding dexamethasone use in COVID-19 published at their journal that remained with NEJM editors from 17 July 2020 until I asked to withdraw it on 30 November 2020 (ID 20-25534), yet I was fortunate to find another journal to review and publish it [14].

My first argument is, as evident in Table 1 of the discussed clinical trial, that 28.1% of the participants in the placebo arm had "missing data" regarding their baseline SARS CoV-2 status compared to only 9.1% in the treatment arm. This missing data should be regarded as a strong confounding factor that could abolish the actual significance of the whole published results.

Second, as also evident in Table 1, it's very suspicious that high risk participants were "randomly" distributed in more percentages, in the placebo arm, in seven major categories and the vice was only noticed in two categories that were relatively small according to their combined percentages (less than 11% of those with high risk factors). Notably, even numeric insignificant variations in effectiveness were previously accepted by the American stakeholders to justify repurposing some very profitable drugs in order to gain an EUA[14] and I claim the current vice argument should, after three years of continuous losses of millions of lives, be considered valid as well, and thus the randomization performed in Brazil, made by "an independent pharmacist" as declared in the article, should be thoroughly questioned.

Third, it's also very bizarre to allow "oral administration" in the placebo arm in a trial testing a parenteral drug and this could also cast huge shadows on the integrity of the claimed "blinding" of this published trial.

Interestingly, two previous USA clinical trials sponsored by Eiger BioPharmaceuticals/ ZymoGenetics using pegylated interferon lambda were discontinued. The first one, NCT04343976, started on June 22, 2020, and was discontinued on October 04, 2021 claiming failure to meet the enrollment goal (14 were recruited from the planned 20 participants) as well as, surprisingly, lack of fund. The other one, NCT04344600, started on June 29, 2020 and was discontinued on September 24, 2021 due to low enrollment (6 were recruited from the planned 164 participants). Notably, only 30 Canadian participants (15 patients and 15 in the placebo arm)

out of previously planned 763 patients (NCT04967430) were involved in the discussed trial [3], to be noted that no data is available to analyze from the discontinued previous trials performed in USA, yet it's very reasonable to suggest that no breakthrough observations were encountered in 2020 and 2021, unlike those claimed in the present one. Notably, in May 2020 Eiger BioPharmaceuticals in collaboration with Icahn School of Medicine at Mount Sinai have planned a phase II study to "test the safety and effectiveness of an investigational drug peginterferon lambda-1a in treating COVID-19" (NCT04388709), yet it was withdrawn in February 2021 claiming that no enrollment was due to competing trials at the site.

Importantly, when Eiger BioPharmaceuticals has once partnered in 2020 with reputable researchers at Stanford University School of Medicine to perform an open-label, single-blind randomized controlled trial where 120 US patients were randomly assigned 1:1 to a single subcutaneous dose of Peginterferon Lambda-1a or placebo along with the standard of care and followed for 28 days, the results showed no difference in duration of SARS-CoV-2 viral shedding and time to symptom resolution when compared with placebo (NCT04331899) as declared by the company on 28 September 2020. However, few days later, on 15 October 2020, the company cherished the results of 60 Canadian patients who were randomized 1:1 to a single subcutaneous dose of Lambda 180 mcg or normal saline placebo and were followed for 14 days, to be noted that when this trial (NCT04354259), called ILIAD, was published at The Lancet Respiratory Medicine, we found the founder of Eiger BioPharmaceuticals as well as other employees among its authors and the principal investigator declares receiving "research support unrelated to this work from Eiger BioPharmaceuticals"[15].

Taken together, I would like to express my rare support to the recent decision made by the American FDA to dismiss a request made by a pharmaceutical company to obtain an EUA for its pegylated interferon lambda to be used, as described in that clinical trial, for patients suffering from COVID-19. Furthermore, I wish to call for a very cautious re-analysis of all the results mentioned in the discussed clinical trial including the reported serious adverse effects.

Finally, I wish to confirm the wisdom of a brilliant published observation, though I disagree with its authors regarding the interpretations leading to its previously mentioned context,: "trials funded by governments and not industry, answering the crucial questions driven by immediate clinician need and not product marketing, and providing data in the spaces of clinical

equipoise—this importance should not be underestimated or lost"[16]. I strongly suggest that our world can no longer withstand any more potential American COVID fiasco similar to that of hydroxychloroquine early granted EUA that was later revoked and other examples that could be later fully exposed.

Ethical Approval

Not applicable

Competing interests

None

Authors' contributions

Sole author

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Availability of data and materials

Not applicable

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