MEDICAL COLLEGE OF WISCONSIN

**8701 Watertown Plan Road**
**Milwaukee, WI 53226**

**Sakti Chakrabarti, M.D.**
**Department of Hematology-Oncology**
**Division of Internal Medicine**
**Phone: 414-805-8292**

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Re: Manuscript ID 05346507

Dear Editors:

On behalf of my coauthors, I am pleased to submit the revised manuscript entitled, “The short term safety of coronavirus disease 2019 (COVID-19) vaccines in patients with solid tumors receiving systemic therapy.” We much appreciate the critiques. We want to express our most sincere gratitude to the reviewers and the editorial team for a thorough review. We have made a sincere effort to address the critiques in our revised manuscript that, we believe, will enhance the value and the clarity of this article.

All edits have been clearly indicated with tracked changes.

Please see below for our point by point response (italicized) to the critique-

## Reviewer 1:

1) Generally, to assess the safety profile of vaccines, we need a longitudinal study design following patients for years. Given the current pandemic it is natural that evidence needs to be floated and provided to the readership. To tackle this, I would highly suggest the authors to change the title to short term safety rather than just safety which is very broad.

Response

*Thank you for this suggestion. We changed the title of the manuscript to “The short term safety of coronavirus disease 2019 (COVID-19) vaccines in patients with solid tumors receiving systemic therapy.”*

*2)* There are multiple studies on solid cancer patients concerning COVID vaccine which the authors failed to cite, acknowledge and discuss. I can place some examples here: 1. Kian W, Zemel M, Kestenbaum EH, Rouvinov K, Alguayn W, Levitas D, Ievko A, Michlin R, Abod MA, Massalha I, Chernomordikov E, Sharb AA, Shalata W, Levison E, Roisman LC, Lavrenkov K, Peled N, Nesher L, Yakobson A. Safety of the BNT162b2 mRNA COVID-19 vaccine in oncologic patients undergoing numerous cancer treatment options: A retrospective single-center study. Medicine (Baltimore). 2022 Jan 14;101(2):e28561. doi: 10.1097/MD.0000000000028561. PMID: 35029223. 2. Lasagna A, Lilleri D, Agustoni F, Percivalle E, Borgetto S, Alessio N, Comolli G, Sarasini A, Bergami F, Sammartino JC, Ferrari A, Zavaglio F, Arena F, Secondino S, Falzoni M, Schiavo R, Lo Cascio G, Cavanna L, Baldanti F, Pedrazzoli P, Cassaniti I. Analysis of the humoral and cellular immune response after a full course of BNT162b2 anti-SARS-CoV-2 vaccine in cancer patients treated with PD-1/PD-L1 inhibitors with or

without chemotherapy: an update after 6 months of follow-up. ESMO Open. 2021 Dec 11;7(1):100359. doi: 10.1016/j.esmoop.2021.100359. Epub ahead of print. PMID: 34973510; PMCID: PMC8664661. 3. Tamura T, Ninomiya K, Kubo T, Kuyama S, Tachibana S, Inoue K, Chikamori K, Kudo K, Ochi N, Harada D, Maeda Y, Kiura K. Short-term safety of an anti-severe acute respiratory syndrome coronavirus 2 messenger RNA vaccine for patients with advanced lung cancer treated with anticancer drugs: A multicenter, prospective, observational study. Thorac Cancer. 2021 Dec 28. doi: 10.1111/1759-7714.14281. Epub ahead of print. PMID: 34964270.

Response

*We have incorporated the suggested studies in our manuscript by referencing them in the discussion section as well as incorporating their key findings in Table 3. However, as the study conducted by Lasgna et al. examined vaccine immunogenicity at the 6-month mark but did not provide a detailed account of the adverse events following vaccination, we have not included this study in our discussion.*

## Reviewer 2:

1) Kindly highlight the novelty of the proposed method in detail. Electronic medical records were accessed to collect information on patient characteristics, systemic therapies, type of vaccine received, and adverse effects associated with the vaccine administration. How records were accessed?

Response

*Thank you for your suggestion. We have incorporated a more detailed account of the methodology of our study in the "Materials and Methods" section (please see below). Additionally, we created a consort diagram (Figure 1) to clarify the patient selection process further.*

2) Discuss more detail about results and experiments.

Response
*We have provided all results that we had on this study. As this study only evaluated short-term adverse effects of the vaccines, we have modified the title accordingly. However, we have added additional text to the discussion section to put the study results in perspective.*

4) Please compare your proposed method with existing methods and show the differences in a table.

Response
*Table 3 has been modified to address this critique.*

5) Figures, diagrams are not sufficient, please add some figures and diagrams. Which increases the quality of the manuscript. Please check the format of text and tables.

Response
*A consort diagram to describe the patient selection has been added (Figure 1). Texts and tables have been modified as well to conform to the journal specification.*

6) Please refer and cite. DOI: 10.1016/j.ipm.2021.102810 DOI: 10.1016/j.chaos.2021.110708 DOI: 10.1016/j.rinp.2021.103813

Response: Appreciate the suggestion. We have added the first 2 references to our manuscript.

## Reviewer 3:

**1) Abstract**

a. Sub sections in the abstract (Background, Aim, Methods, Results and Conclusion) should use the same section names from the manuscript. There is discrepancy (such as **Introduction**- used in the manuscript) and there is no Aim or Objectives section in the manuscript. Please work on using similar section/sub-section names?

b. Result subsection- please use the logical order. (Mention the type of cancers before the type of vaccines used)

c. It is recommended to use **similar** format and **the standard one** in writing numbers and their percentages throughout the text. Please remove messy and unattractive mixed styles. (*Taxane-based regimens (14.2%), BNT162b2 by Pfizer (110/210, 52%), gastrointestinal 43.8% (92/210), 53 grade 1 (85%), second dose (37, 59.7%).*

Response

*Thank you for your constructive suggestions.*
*We followed the retrospective cohort study template as specified by the journal. We have also added the aim of our study as suggested.*

*For suggestion number (2), the result subsection of the abstract was re-organized to mention types of cancers before types of vaccine used.*

*For suggestion number (3), we standardized numerical statistic documentation throughout the text.*

**2) Introduction**

1. Please mention about the biology of solid tumor and the available treatment options. Give some details related solid tumors and the treatment modalities.

2. Please mention previous studies in the area; their findings and limitations/gap in the use of COVID-19 vaccines. If none mention it too.

Response

*In regards to suggestion (1), we incorporated information concerning solid tumor malignancies and treatment options in the introduction.*

*In regards to suggestion (2), we highlighted multiple studies and their findings both in our discussion section and in table 3.*

**3) Materials and Methods**

1. Which cancer center database/s were used?? (mention in the text)

2. Why 1 month duration is selected and any justification???
3. The severity or stage of the disease is not considered in the inclusion/exclusion criteria. It is obvious that severity of disease and presence of other co-morbidities might affect the outcomes results. How are these factors addressed in this study???
4. Please provide citation for “version 5.0 of the Common Terminology Criteria for Adverse Events”.
5. Any exclusion criteria??
6. Please mention about the statistical tests/analysis used??

Response

*Thank you for these suggestions. In regards to number (1), we clarified which database was used in the methods section.*

*In regards to suggestion (2), electronic charts were reviewed for a 1-month duration following the second vaccination to catch the short-term adverse effects. The study was not designed to evaluate long-term adverse effects.*

*In regards to suggestion (3), the correlation between the severity/ stage of disease and adverse effects of the vaccine was not analyzed as a much larger prospective study would be required to explore this aspect.*

*In regards to suggestion (4), a citation was added for “version 5.0 of the Common Terminology Criteria for Adverse Events”.*

*In regards to suggestion (5), exclusion criteria for the study were added in the Materials and Methods section. Additionally, we have incorporated a more thorough analysis of the methodology of the study in this section. We also created a consort diagram to clarify the patient selection process further.*

*In regards to suggestion (6), our study was a single-arm, retrospective observational study to catch the short-term adverse effects of the vaccine, and hence any statistical analysis was not included.*

**4) Results**

1. Writing of numbers and percentiles is again messy which needs correction and uniform presentation trough out the text.
2. Why is the statistical analysis limited to descriptive only?? no further statistical tests like Odds Ratio or Correlation coefficients or others considered?
3. All information in Table 1 is described in the text paragraphs. Why it is needed to repeat?
4. Regarding Table 2, remove information’s already mentioned in the text and use similar format of expression again.
5. Remove Table 3. Studies shown in table 3 were already mentioned in the text. Avoid redundancy. In addition, such separate table of studies (which is commonly used in systematic review) is not usual in cohort studies like this study.

Response

*In response to suggestion (1), we standardized the writing of numbers and percentages throughout the text.*

*In regards to suggestion (2), our study was a single-arm, retrospective observational study to catch the short-term adverse effects of the vaccine, and hence any statistical analysis was not included.*

*In regards to suggestions (3), (4), and (5), we summarized the data in a table as many busy readers may not read the text.*

**5) Discussion**

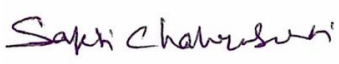
1. Paragraph two (starting from “The pandemic caused by the novel coronavirus……” to “…….undergoing active cancer treatment.”) is more general and basic description, which is better to be moved to introduction section. Here, discussion should focus on relating specific results with other study results in detailed manner.

Response

*Thank you again for the insightful critique. Regarding suggestion (1), while we understand your reasoning for transposing this information to the introduction, we included a general description to highlight the magnitude and rigor of the problem to put our research into perspective.*

We look forward to receiving your response.

Sincerely, on behalf of my coauthors,



Sakti Chakrabarti, M.D.
Associate Professor