Discussion to: Use of a novel microbiome modulator improves anticancer immunity in a murine model of malignant pleural mesothelioma

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PII: S2666-2736(24)00048-2
DOI: https://doi.org/10.1016/j.xjon.2024.02.013
Reference: XJON 1021

To appear in: JTCVS Open

Received Date: 22 February 2024
Accepted Date: 22 February 2024

Please cite this article as: Chriqui LE, Donington J, Perentes JY, Discussion to: Use of a novel microbiome modulator improves anticancer immunity in a murine model of malignant pleural mesothelioma, JTCVS Open (2024), doi: https://doi.org/10.1016/j.xjon.2024.02.013.

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Discussion to: Use of a novel microbiome modulator improves anticancer immunity in a murine model of malignant pleural mesothelioma

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Disclosures: None

Dr. Jessica Donington (Chicago, IL):

Thank you. And thank you Dr. Chriqui for sending me your manuscript in such a short amount of time. I very much appreciate it, and I very much enjoyed it. It's very well-written. I want to congratulate you and your investigators for Lucerne on this really interesting work. I also want to congratulate you on your title. You did a wonderful job of using shock and awe to really get the program committee's attention. While this a prebiotic distilled from a spent brewery grain, somehow beer sludge was a little more intriguing. That, or we all like the thought of drunk little mice running around in the labs. There is definitely growing prominence and evidence for the impact of the microbiome on tumor progression, and its manipulation in helping to treat and cure these cancers. We know with the use of immunotherapies that the gut microbiome signatures can predict not only response to therapy but how to deal with toxicities. Most of this work to date, though, isn't as you have shown us in diseases such as colon
melanoma, and even in lung. A little less than what we might call sterile areas, like the pleural space. But that being said, I think many of us see mesothelioma as a disease highly impacted by inflammation, and therefore, really prone to this area of investigation. There is very little out there in terms of manipulating the microbiome to treat mesothelioma. And yet, it's so attractive due to its ease of accessibility, not only as a biomarker but for manipulation. You have really shown a promising result in terms of manipulating cytotoxic T cell activity in your immunocompetent mouse mode, so congratulations.

You presented a little more data here than I saw in the manuscript provided to me. Because after reading what I had, my first real question dealt with, what are you thinking about, and can you pair this with CTLA-4 and PD-L1 agents? Have you looked at your effect in pairing with both of them since Ipi/Nivo is an approved treatment for mesothelioma?

Dr. Louis-Emmanuel Chriqui (Lausanne, Switzerland):

Okay, thank you. Thank you for your comments. For the title, I would like to give the credit to my PI, who always comes up with great ideas like this. So, thanks to him. Regarding your question on the drug combination. Yes, it's definitely the next step. We would like, first, to have some insight on the expression of CTLA-4 and PD-L1. And now we are getting this data, we will move to the combination to be closer to the current standard of care. Yes, exactly.

Dr. Donington:

And that your model - which I do really like quite a bit - is a sarcomatoid?

Dr. Chriqui:

No, it's a biophysic model.

Dr. Donington:

It's a biophysic, okay. And we would need a new-- that is your only cell line right now that is synergetic in the BALB mice?

Dr. Chriqui:

The BALB mice are the only one we have. Well, yes, it's the only one. We have two other models. We would like also to investigate a few models to repeat the study.
Dr. Donington:

And I guess I'm also wondering-- we talk a lot about T cells, but B cells play a big role in the gut immune system, too. Did you see differences in B cell populations? And would your new mice population be a great place to study that?

Dr. Chriqui:

So, we focused, first, on the T cell, and gave interest to combine it with immunotherapy. But yes, it's emergent to pick B cells are really get interest in its next step. Thank you for your comment to investigate it, yes.

Dr. Donington:

And I think I really like-- I'm looking forward to seeing your work looking maybe more at what's definitely happening directly in the gut, in the stool, are there specific species that can answer some mechanistic questions here.

Dr. Chriqui:

Yes, exactly. Yeah.

Dr. Donington:

Very nice work. Thank you.

Dr. Chriqui:

Thank you.