

Study suggests changing the gut microbiome improves health outcomes for newly-diagnosed metastatic kidney cancer

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Physician scientists from City of Hope, one of the largest cancer research and treatment organizations in the United States, found that people with metastatic kidney cancer who orally took a live biotherapeutic product called CBM588 while in treatment with immunotherapy and enzymatic tyrosine kinase inhibitors experienced improved health outcomes.

The [Phase I trial](#) was [published](#) in *Nature Medicine*.

Microorganisms in the gut modulate the [immune system](#). City of Hope researchers are now in discussions with the global SWOG Cancer Research Network to design a Phase II/III trial to assess the City of Hope-identified novel use of CBM588 and microbiome modulation in people with advanced cancer.

Sumanta Pal, M.D., professor and vice chair of academic affairs in City of Hope's Department of Medical Oncology & Therapeutics Research, is slated to be co-leader of the potential Phase II/III SWOG trial.

"We at City of Hope are the first to demonstrate a live bacterial product's ability to improve [clinical outcomes](#) for patients with kidney cancer treated with immunotherapy. CBM588 could be exciting in [cancer treatment](#) because of its potential to enhance the efficacy of immune checkpoint inhibitor-based treatment, improve patient outcomes

and modulate the [gut microbiota](#) in beneficial ways," said Pal, a City of Hope medical oncologist and corresponding author of the new study.

"Ongoing and larger clinical trials are crucial to validate these benefits and address current challenges. If the positive results observed in this small trial and a previous trial with nivolumab and ipilimumab are confirmed, CBM588 could become a valuable supplement in the treatment of various cancers, particularly for patients treated with immune checkpoint inhibitors."

An [estimated 44% of U.S. patients](#) with cancer in 2018 were eligible for checkpoint inhibitor drugs, according to a *JAMA Network Open* article that flags the increasing trend of this percentage.

In the single-center, Phase I trial, 30 people with metastatic kidney cancer were randomized to receive cabozantinib, an inhibitor of vascular endothelial growth factor receptor, and [targeted immunotherapy nivolumab](#) with or without CBM588 as first-line treatment. Participants' gut microbiome were analyzed via stool samples in the beginning for a baseline and then 13 weeks into treatment.

City of Hope has granted an exclusive worldwide [license to Osel for intellectual property](#) on the novel use of CBM588 to enhance the efficacy of checkpoint inhibitors used to treat cancer, including metastatic renal cell carcinoma. Scientists from Osel and Miyarisan Pharmaceutical Co. Ltd, the manufacturer of CBM588, collaborated on the study.

To date, many studies on lung cancer, melanoma and [metastatic kidney cancer](#), among other diseases, have shown that the composition of the gut microbiome could predict immunotherapy outcomes for patients with cancer.

Current guidelines for metastatic renal cell carcinoma ([kidney cancer](#)) recommend that newly diagnosed patients receive either dual checkpoint inhibitor therapy or a combination of immunotherapy and tyrosine kinase inhibitor, but most patients eventually experience disease progression while on treatment.

Positive patient outcomes usually do not last, and subsequent treatments are largely palliative rather than curative. So, physician scientists are looking to combine current strategies with new treatments that do not introduce toxic side effects, such as through microbiome modulation.

In the trial, City of Hope researchers observed an increase in the abundance of unclassified Ruminococcaceae genera, which has been linked with improved clinical outcomes with immune checkpoint inhibitors in recent studies. *Clostridium butyricum* MIYAIRI 588, the bacterium in CBM588, produces butyric acid, which is critical for intestinal health and is a well-known immunomodulator.

"While not yet part of standard cancer treatment protocols, microbiome modulation is a promising area of research with the potential to enhance the efficacy of cancer therapies, particularly immunotherapies. Current applications are primarily within [clinical trials](#), but the growing body of evidence suggests that microbiome-based interventions may soon become a valuable component of cancer treatment strategies," said Hedyeh Ebrahimi, M.D, M.P.H., City of Hope postdoctoral medical oncology fellow and first author of the study.

City of Hope is accelerating its research on the direct link between a healthy gut and the effectiveness of immune therapies, such as CAR T cell therapy. Its enhanced microbiome program spans from basic to clinical research and includes studying the gut microbiome's role in protecting transplant patients from complications experienced during their recovery.

"This study demonstrates again that the microbiome has an important role in the efficacy and toxicity of cancer immunotherapy and can be targeted to improve outcome," said Marcel van den Brink, M.D., Ph.D., president of City of Hope Los Angeles and City of Hope National Medical Center, and the Deana and Steve Campbell Chief Physician Executive Distinguished Chair.

More information: Cabozantinib and nivolumab with or without live bacterial supplementation in metastatic renal cell carcinoma: a randomized phase 1 trial, *Nature Medicine* (2024). [DOI: 10.1038/s41591-024-03086-4](https://doi.org/10.1038/s41591-024-03086-4)

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