

## Antibody could be used to target tumor-causing protein, study shows

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Cincinnati Cancer Center (CCC) and University of Cincinnati (UC) Cancer Institute researchers have found in a phase-1 study that patients with advanced melanoma and kidney cancer who were treated with a certain antibody that targets a tumor-enhancing protein was safe, which could lead to more treatment options for patients.

The study is published in the March 11 edition of *PLOS ONE*, a peer-reviewed, open access online publication.

Principal Investigator John Morris, MD, clinical co-leader of the Molecular Therapeutics and Diagnosis Program for the CCC, co-leader of the UC Cancer Institute's Comprehensive Lung Cancer Program, professor in the division of hematology oncology at the UC College of Medicine and UC Health medical oncologist, says this study sheds light on a therapy that could be used alone or in combination to help [patients](#) with a number of cancers.

"Transforming growth factor-beta (TGF $\beta$ ) is a protein that helps cells maintain their functions, from formation to transition to death," Morris says. "Early in the transition of cancers from premalignancy to malignancy, TGF $\beta$  can suppress cell growth; however, in advanced cancers, these effects are typically lost, and TGF $\beta$  will directly promote the growth and spread of tumors.

"TGF $\beta$ -caused cellular changes have been described in many different tumor models and appear to be important for causing cell migration and

promoting spread of [cancer](#). Increased TGF $\beta$  has been reported in many different cancers including prostate, breast, lung, pancreatic, renal cell, or kidney, liver and more, and elevated plasma TGF $\beta$  levels correlate with advanced tumor stage, metastases and poor survival. Given this data, the protein is being examined for potential therapeutic targets."

He adds that in preclinical models, using antibodies or receptors that hinder TGF $\beta$  have shown [antitumor activity](#).

"In animal models, effects of anti-TGF $\beta$  combined with various chemotherapies, radiation or other biologic-related treatments, including vaccines, have been reported to improve the treatment of both primary and metastatic disease," Morris says. "GC1008, or fresolimumab, is a human antibody that neutralizes the active forms of human TGF $\beta$ .

"GC1008 was investigated as a treatment for cancer and fibrotic diseases. We wanted to test the safety of this treatment in repeated doses for patients with malignant [melanoma](#) (skin cancer) and renal cell carcinoma ([kidney cancer](#))."

In the study, which was conducted at the National Cancer Institute and a number of cancer centers in the U.S., patients with previously treated malignant melanoma or renal cell carcinoma received intravenous GC1008 at varying doses. Patients who were stabilized, with no progression of the cancer, were eligible to receive extended treatment consisting of four doses of GC1008 every two weeks for up to two additional rounds.

Pharmacokinetic and exploratory biomarker assessments were performed.

"Twenty-nine patients, 28 with malignant melanoma and one with [renal cell carcinoma](#), were enrolled and treated with 22 in the dose-escalation

portion and seven in a safety cohort arm, with one consistent dose delivered," Morris says. "No dose-limiting toxicity was observed, and the maximum dose, 15 mg/kg, was determined to be safe."

He adds that four patients developed reversible squamous-cell carcinomas (a type of skin cancer), one [malignant melanoma](#) patient experienced a partial positive response to treatment and six had stable disease with a progression-free survival of 24 weeks.

"GC1008 showed an acceptable safety profile when administered up to 15 mg/kg every two weeks," Morris says. "This preliminary evidence of antitumor activity indicates that additional studies are needed to help determine the efficacy and safety of GC1008 alone and in combination with other treatments, as well as define dose and response."

Provided by University of Cincinnati Academic Health Center

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