Study examines use of toad venom in cancer treatment

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Huachansu, a Chinese medicine that comes from the dried venom secreted by the skin glands of toads, has tolerable toxicity levels, even at doses eight times those normally administered, and may slow disease progression in some cancer patients, say researchers from The University of Texas M. D. Anderson Cancer Center.

The results from the Phase I clinical study, a collaborative research project between M. D. Anderson and Fudan University Cancer Hospital in Shanghai, are reported in the online Early View feature of the journal *Cancer*. The study marks the first time a formal clinical trial has examined the relationship between huachansu dose and toxicity, although the drug is common in China and approved by the Chinese Food and Drug Administration.

Huachansu is widely used to treat patients with liver, lung, colon and pancreatic cancer at oncology clinics in China. Chinese clinical trials conducted since the 1970s have demonstrated the anti-cancer properties of huachansu, citing total response rates of 10 percent and 16 percent observed in patients with advanced hepatocellular carcinoma and lung cancer, respectively[1,2].

"Studying traditional Chinese medicine such as huachansu is new to American research institutions, which have been skeptical and slow to adopt these complementary treatments. However, it is important to understand its potential role in treating cancer," says Lorenzo Cohen, Ph.D., one of the paper's authors and director of the Integrative

Medicine Program at M. D. Anderson. "We wanted to apply a Western medicine-based approach to explore the role of the toad venom compound in cancer patients and test if it is possible to deliver a more potent dose without raising toxicities or side effects."

The clinical trial was conducted at the Fudan University Cancer Hospital while M. D. Anderson provided training and ongoing consultation. The institutions collaboratively designed the trial that was approved by both institutional review boards. M. D. Anderson and Fudan University Cancer Hospital signed a sister institution agreement in 2003, creating a framework for research, educational and clinical collaboration.

The typical dose of huachansu used in China is approximately 15 milliliters of drug per meter squared of body mass (mL/m2). In the study, 15 patients with stage III or IV hepatocellular (liver) carcinoma, nonsmall cell lung cancer or pancreatic cancer received one of five dose levels ranging from 10 mL/ m^2 up to 90 mL/m^2 from January 2005 through July 2006. The treatment was repeated daily for 14 days followed by seven days off (one cycle). After two cycles, most patients received other treatments. Quality control methods were put in place to ensure huachansu of a uniform and consistent lot.

While the dose was up to eight times higher than conventional doses used in China, researchers observed only low toxicities or side effects. Eleven (73 percent) patients had no toxicities greater than the lowest grade measured. Importantly, no significant cardiac toxicity was observed and no significant changes in cancer-related symptoms occurred. Of the 15 patients who completed the treatment, six hepatocellular carcinoma patients (40 percent) had stable disease for a median of six months. One patient had a 20 percent reduction in tumor mass that lasted for more than 11 months.

"Even though we saw no complete or partial response (reduction of

disease by 30 percent or more) it is encouraging that the cancer did not progress in a large set of the hepatocellular carcinoma patients," says Zhiqiang Meng, principal investigator on the trial and an associate professor and deputy chair of the Department of Integrative Oncology at Fudan University Cancer Hospital, "Previous observations from studies conducted in China have shown that huachansu can inhibit tumor cell growth and improve immunologic function[3]. These findings, coupled with that knowledge, demonstrate the need for further clinical trials of this promising agent."

A Phase II clinical trial comparing the effects of huachansu combined with gemcitabine (Gemzar®) to gemcitabine and placebo for patients with advanced pancreatic cancer is under way at the Fudan University Cancer Hospital in collaboration with M. D. Anderson.

More information:

1 Hang L. Clinical effect of Huachansu injection in combination with chemotherapy in advanced lung cancer. Henan J. Oncol. 2002; 15.

2 Zhongjie S, Chengen P, Guojin W. Clinical observation on Huachansu in treating hepatocellular carcinoma after transarterial chemoembolization (TACE). Zhong Liu Fang Zhi Za Zhi. 2002;29:67-69.

3 Chen GH. Advances in quality determination, pharmological studies and clinical application of toad venom. Chin Tradit Herb Drugs, 2001;32:184-186.

Source: University of Texas M. D. Anderson Cancer Center (news : web)