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Cancer News

Immunoembolization safe, promising for liver metastases from uveal melanoma



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NEW YORK (Reuters Health) - A novel immunoembolization therapy using granulocyte-macrophage colony-stimulating factor (GM-CSF) safely achieved regression of unresectable liver metastases from uveal melanoma, according to a phase I study by U.S. researchers, published online by the Journal of Clinical Oncology.

Immunoembolization is a variation of chemoembolization, which involves infusing a cytotoxic agent into a tumor after mechanically or surgically disrupting the tumor's blood supply. (Most often, hepatic artery chemoembolization is performed to control hepatocellular carcinoma.)

Theoretically, the authors explain, the advantage of immunoembolization is that it could attract and stimulate antigen-presenting cells in liver tumors and improve the uptake of tumor antigens released from necrotic tumor cells, as well as potentially facilitate a systemic immune response against tumor cells and thereby suppress the growth of extrahepatic metastases.

Furthermore, recombinant human GM-CSF (these researchers used sargramostim) has been shown to stimulate macrophages and to increase the cytotoxicity of monocytes toward malignant melanoma cells in vitro.

"As long as patients do not have any extra-hepatic metastasis, or as long as extra-hepatic metastases are small or controlled, our approach should work for other types of melanoma," Dr. Takami Sato of Thomas Jefferson University, Philadelphia, told Reuters Health.

The study cohort comprised 39 patients, including 34 who had primary uveal melanoma. Uveal melanoma can be effectively treated, but once it metastasizes to the liver, survival can be less than 6 months.

At 4-week intervals following hepatic artery embolization, patients received escalating doses of GM-CSF, beginning with 25 µg. Even at doses up to 2,000 µg, the maximum tolerated dose was not encountered, and the majority of patients receiving that dose reported only mild adverse effects (fever, upper abdominal pain and nausea) for 1 or 2 days. There were no treatment-related deaths.

Among the 31 patients with primary uveal melanoma who were assessable by radiography, 2 patients had complete response, 8 had partial responses and 10 had stable disease.

The median overall survival under an intent-to-treat approach was 14.4 months. One- and 2-year survival rates were 62% and 26%, respectively. The mean survival rate among patients who achieved complete or partial responses was 33.7 months. One patient was still alive at 40.8 months of follow-up.

Patients who received higher doses of GM-CSF (1,500 µg or more) had longer progression-free survival than those receiving lower doses (1,000 µg or less, P = 0.006).

The researchers note that a phase II randomized, double-blind trial comparing

embolization with and without GM-CSF is already underway.

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2318 Mill Road, Suite 800, Alexandria, VA 22314 | phone: (571)483-1300
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