A Alternative Medicine
AN EVIDENCE-BASED APPROACH

Avmear as Supportive Therapy in Cancer

The Extract and Its Effects

An extract of fermented wheat germ, Avmear, was developed during the 1990s by Hungarian biochemist Mate Hidvegi, Ph.D. Initially, Avmear was available as an over-the-counter dietary supplement, but in 2002 the product was developed as a nutritional adjunct by the Hungarian National Institute of Food Safety and Nutrition.

“Although it is not like shark cartilage or cat’s claw or other such products, which may or may not be good, but which are not official cancer treatments,” Dr. Hidvegi said in an interview. For example, the Hungarian Association of Oral and Maxillofacial Surgeons has issued an official statement indicating that Avmear should be included in the treatment protocol for squamous cell carcinoma of the oral cavity.

Avmear is manufactured by Biromedica Co., Budapest, and is marketed in the United States by American BioSciences Inc., Blauvelt, N.Y.

The precise molecular targets by which Avmear produces its immunomodulatory effects have not yet been identified, but Dr. Hidvegi and colleagues have proposed several possibilities. Experiments have shown that Avmear inhibits the growth of leukemia cells by inducing apoptosis through activation of the caspase-3-catalyzed cleavage of the poly(ADP-ribose) polymerase (PARP) enzyme. The result of this is that the cells are selectively sensitized to drugs such as 5-fluorouracil (Ann. N.Y. Acad. Sci. 2005;1051:529-42).

Avmear also decreases the amount of the major histocompatibility complex I proteins on tumor cells, which may increase the tumor cells’ exposure to natural killer cells and thereby reduce their metastatic activity (Int. J. Oncol. 2002;20:563-70). It also upregulates the expression of intercellular adhesion molecule-1 on tumor-derived endothelial cells and potentiates the effects of tumor necrosis factor-α (Ann. N.Y. Acad. Sci. 2005;1051:515-28).

In vivo immunomodulatory effects of Avmear were seen in experiments on mice showing that the compound increased the degree of blastic transformation of peripheral blood T lymphocytes stimulated by the mitogen concanavalin A. In other animal studies, immunocompromised mice that had undergone thymectomy showed improved survival by not rejecting skin grafts when treated with the extract (Immunopharmacology 1999;41:183-6).

Clinical Studies

Two small, open-label pilot trials found that Avmear was associated with inhibition of disease progression and improved survival in patients with advanced colorectal cancer. A multivariate analysis of phase III study, also open-label, then was undertaken at three oncology centers in Hungary. Following radical surgery plus radiotherapy and/or chemotherapy, patients were randomized to receive the option of taking Avmear; 66 did so and 104 patients who declined the treatment served as controls.

At baseline, control patients were older, but disease stage was worse in the Avmear group. Twenty-seven percent of patients in the treatment group had stage IV metastatic cancer, compared with only 8.8% of those in the control group. The Avmear cohort also had a longer time lag from diagnosis to the start of chemotherapy than the control group.

The treatment consisted of 9 mg of Avmear dissolved in 150 mL of water once daily.

The end-point analysis, with follow-up extending to 70 months, showed that progression-related events including new recurrent disease, new metastases, and deaths occurred significantly more frequently in the control group. A total of 16.7% of patients in the Avmear group experienced any progression-related event, compared with 42.3% of those in the control group (Br. J. Cancer 2003;89:465-9).

No serious adverse events were associated with the treatment. The most common side effects were gastrointestinal disturbances.

Avmear also has been evaluated in patients with stage III melanoma by a group of Russian investigators. In their presentation at a 2002 congress of the International Union Against Cancer in Oslo, Norway, Avmear was linked to benefits in terms of progression-free survival in a group of postsurgical patients.

A total of 46 patients received dacarbazine, 400 mg/m² body surface in cycles of 5 consecutive days, repeated monthly for up to 4 months or until disease progression. In this group, 22 received 9 g Avmear daily during treatment and for 12 months afterward. At 12 months, 75% of the control group had experienced disease progression, compared with 36.3% of the Avmear group. “We now have 3-year follow-up data, again showing statistically significant benefits in progression-free survival and overall survival for the Avmear patients,” said Dr. Hidvegi, who is honorary professor at the Budapest University of Technology and Economics as well as at the Jewish University in Budapest, and is now chairman of Biromedica.

Another pilot study evaluated the effects of the wheat germ extract on chemotherapy-induced febrile neutropenia in a group of 22 children with a variety of solid tumors. All patients received standard chemotherapy, and half also received Avmear, 6 g/m² twice daily. Evaluations took place at baseline, at the end of the first month, and every 3 months thereafter.

“The chemotherapy protocol used for children with solid tumors is high dose and very myelotoxic, so although these cancers are 100% curable, the patients are susceptible to infections and some even die,” Dr. Hidvegi said. A total of 30 episodes of febrile neutropenia occurred in the active treatment group during a total of 121 cycles of chemotherapy (24.8%), whereas 46 episodes occurred during the 106 cycles (43.4%) completed by the control group, a difference that was statistically significant (J. Pediatr. Hematol. Oncol. 2004;26:631-5). The study showed that Avmear was usefully feasible, with no significant side effects of chemotherapy, Dr. Hidvegi said.

By Doug Brunk
San Diego Bureau

More Herbal Therapies Entering Clinical Trials

BY DOUG BRUNK
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La Jolla, Calif. — An emerging trend in complementary and alternative medicine is a shift away from animal-only studies and toward clinical trials involving the use of herbs for cancer treatment. Dr. Mary L. Hardy said a meeting on natural supplements in evidence-based practice sponsored by the Scripps Clinic.

“I really want to see if we can get out of mice and into humans for some of these interesting herbs for cancer, and I think we will,” said Dr. Hardy, associate director of the Center for Dietary Supplement Research in Botanicals at the University of California, Los Angeles.

She discussed an ongoing study of 82 patients with oral leukoplakia who underwent micronuclei and chromosomal assays and then were treated with 4.5 cups a day of black tea for 1 year (J. Environ. Pathol. Toxicol. Oncol. 2005;24:141-4).

The researchers repeated the micronuclei assay at 6 months and the chromosomal assay at 12 months. Of the 15 patients who completed the study, all showed a significant decrease in micronuclei frequency and chromosomal aberrations. “This is not a toxic or difficult intervention,” Dr. Hardy noted at the meeting, which was cosponsored by the University of California, San Diego.

She also predicted that there will be an increasing number of studies of pomegranate juice and other anthocyanin-enriched juices for a variety of conditions, particularly cardiovascular disease. In one recent trial, 45 patients with coronary artery disease and ischemia were randomized to receive 240 mL pomegranate juice daily or placebo for 3 months (Ann. J. Cardiol. 2005;96:810-4). Patients underwent CT scintigraphy at rest at baseline and 3 months.

Scan results showed that stress-induced ischemia decreased in the patients who drank the pomegranate juice but increased in those who did not drink it, said Dr. Hardy, who also directs the Integrative Medicine Group at Cedars-Sinai Medical Center, Los Angeles.

Use of traditional Chinese herbs in clinical trials for a variety of conditions also is on the rise. In one recent trial, Japanese investi-