ALTERNATIVE MEDICINE
AN EVIDENCE-BASED APPROACH

Avemar as Supportive Therapy in Cancer

The Extract and Its Effects

An extract of fermented wheat germ, Avemar, was developed during the 1990s by Hungarian biochemist Mate Hidvegi, Ph.D. Initially, Avemar was available as an over-the-counter dietary supplement, but in 2002 the product was registered as a medical nutriment with an indication for use in cancer treatment by the Hungarian National Institute of Food Safety and Nutrition.

"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. In Hungary, Avemar has become an accepted part of cancer treatment," Dr. Hidvegi said in an interview. For example, the Hungarian Association of Oral and Maxillofacial Surgeons has issued an official statement indicating that Avemar should be included in the treatment protocol for squamous cell carcinoma of the oral cavity.

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

The precise molecular targets by which Avemar produces its immunomodulary effects have not yet been identified, but Dr. Hidvegi and colleagues have proposed several possibilities. Experiments have shown that Avemar 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).

Avemar also decreases the amount of the major histocompatibility complex class 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 Avemar 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 immune function 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 Avemar was associated with inhibition of disease progression and improved survival in patients with advanced colorectal cancer. A multicenter phase III study, also open-label, then was undertaken at three oncology centers in Hungary. Following radical surgery plus radiotherapy and/or chemotherapy, patients with colorectal cancer were given the option of taking Avemar; 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 Avemar group; 27.3% of patients in the treatment group had stage IV metastatic cancer, compared with only 3.8% of those in the control group. The Avemar cohort also had a longer time lag from diagnosis to the start of therapy and less previous radiotherapy. The treatment consisted of 9 mg of Avemar dissolved in 150 mL of water once daily.

► *An extract of fermented wheat germ has shown immunomodulatory effects in vivo and tumor-suppressive effects in vitro.*

► *Studies conducted primarily in Eastern Europe have suggested that the proprietary formulation Avemar may be beneficial in certain types of cancer.*

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 Avemar 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.

Avemar 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, Avemar 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/m^2 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 Avemar 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 Avemar group. "We now have 3-year follow-up data, again showing statistically significant benefits in progression-free survival and overall survival for the Avemar 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 Biromedicina.

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 Avemar, 6 g/m^2 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 myelosuppressive, 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 patients in the control group, a difference that was statistically significant (J. Pediatr. Hematol. Oncol. 2004;26:631-5). The study showed that Avemar was useful for ameliorating the serious side effects of chemotherapy, Dr. Hidvegi said.

—Nancy Walsh

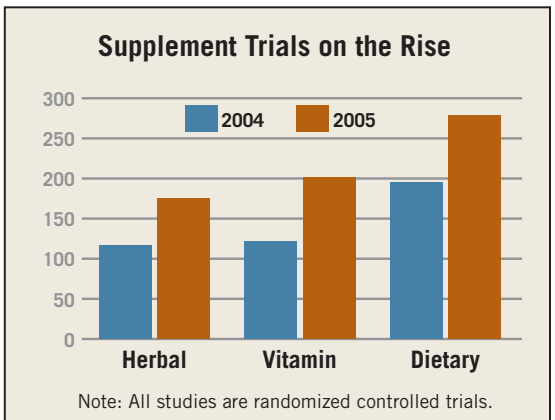
More Herbal Therapies Entering Clinical Trials

BY DOUG BRUNK
San Diego Bureau

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 daily for 1 year (J. Environ. Pathol. Toxicol. Oncol. 2005;24:141-4).



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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 (Am. 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 investigators randomized 52 patients with dementia to receive the traditional Chinese medicine Yi-Gan San or a placebo for 4 weeks (J. Clin. Psychiatry 2005;66:248-52). The mean patient age was 80 years, and 28 of the patients were women. Dr. Hardy described Yi-Gan San as a water-based decoction of seven herbs.

The researchers recorded significant improvements in behavioral symptoms and activities of daily living in patients who took Yi-Gan San, compared with those in the control group. ■

Reagent Recalled: Screening Tests for Over 40 Disorders Could Be Inaccurate

A diagnostic reagent has been recalled because it may produce a weak signal that could translate into inaccurate results for tests used to screen more than 40 disorders.

The reagent is used with the Vitros Immunodiagnostic ECi/ECiQ System to diagnose conditions such as cardiac disease, hepatitis (A, B, or C), thyroid disorders, HIV, and pregnancy. The recall affects lots #8350 and #8530.

Customers with affected lot numbers should not use any remaining reagent and should follow the enhanced Quality Control procedure provided for each pack in all lots until further notice.

Patients who have had any diagnostic tests in the last 60 days and are concerned about their test results should discuss their results with their physician. Those with questions should contact Judy Strzepek of Ortho-Clinical Diagnostics Inc. by calling 908-218-8524.

—Kerri Wachter