

# Oncology Week

## In Review

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## Women Who Hit the Road During Breast-Cancer Therapy Stay Fit

**OTTAWA**—Exercise ad libitum during adjuvant therapy for early breast cancer seems to fight off fatigue and feelings of dependence.

An oncology rehab group here found that women asked to exercise on their own during therapy got a jump start toward keeping themselves from sinking into a physical and emotional funk.

The exercisers—many taking potentially cardiotoxic doxorubicin—did significantly better in cardiac and overall conditioning than those advised to rest to relieve the weight of the arduous therapy, Dr. Roanne Segal, medical director of the Ottawa Regional Cancer Center, and colleagues reported in the Feb. 1 *Journal of Clinical Oncology*.

Among 123 women with Stage I or II breast cancer, those randomized to walk for an hour on their own three to five times a week had a 5.7-point increase in physical functioning from baseline after 26 weeks.

Surprisingly, women randomized to the same exercise in a supervised group setting three times a week had only a 2.2-point increase. Controls were women getting usual care—advice from physicians to participate in exercise if they felt up to it. These women, as a group, had a 4.1-point drop in physical functioning.

The researchers had expected supervised exercise to yield better results than self-directed exercise. The difference, they said, could be attributed to the convenience of home exercise and the freedom to increase exercise intensity when out of a structured setting.

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## IG: Medicare Pays \$1 Billion Too Much For Cancer-Drug Reimbursement

**WASHINGTON**—The government has fired a new salvo in its effort to trim chemotherapy-drug reimbursement to oncologists.

The HHS inspector general issued a report late last month calculating that Medicare would save \$1.6 billion of its annual \$3.1-billion outlay for 24 drugs, most of them for cancer, if it bought the drugs directly from manufacturers and wholesalers—the way the VA system does.

The VA paid from 8% to 91% less for the 24 drugs than Medicare, which reimburses physicians at 95% of the average wholesale price, said the IG's report. For 12 of the drugs, HCFA paid more than twice as much as the VA.

The IG estimated that Medicare payments for 24 drugs exceeded actual wholesale prices by \$761 million a year, representing 25% of the \$3.1 billion Medicare paid in 1999. Actual wholesale prices were between 6% and 84% below Medicare reimbursement amounts for the 24 drugs, the IG said. Four of the drugs had median catalog prices that were less than half the Medicare amount. One of these drugs had a Medicare reimbursement amount more than six times higher than the median catalog price.

“Medicare simply pays too much for prescription drugs,” the report declared.

Nevertheless, the IG's report is likely to have little impact, at least in the near future. The report acknowledged that it didn't take into account the argument by oncologists that any excess reimbursement for drugs was needed to offset

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## In the Pipeline...

### Phenoxiodiol into phase-1b

**Novogen** of Stamford, Conn., has received FDA clearance to start a phase-1b trial of phenoxiodiol for advanced prostate cancer and other advanced solid tumors. This recommendation is based on results of a phase-1a trial in Australia. According to the company, the agent has properties that include antiproliferation, induction of differentiation, and induction of apoptosis. It also seems to downregulate androgen production.

### IMC-C225 on fast track

**ImClone** of New York announced it has received the FDA's fast-track review status for IMC-C225, a monoclonal antibody that inhibits epidermal growth factor receptor expression, for refractory colorectal cancer. The agent is in phase-2 trials. The company is also investigating it for head-and-neck and pancreatic cancer.

### Magnetic doxorubicin delivery an orphan

**FeRx** of San Diego said it received orphan-drug designation from the FDA for MTC-DOX for primary liver cancer. The agent, in phase-2 trials, delivers doxorubicin to tumor cells through the company's Magnetic Targeted Carriers. When a magnetic field is applied to the body, these microparticles, which contain iron, transport the drug to the lesions.

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## Glioblastoma Multiforme Responds to Dendritic-Cell Immunotherapy

**LOS ANGELES**—Autologous dendritic-cell vaccines have been extended to glioblastoma multiforme.

Riding on the early promise of the immunotherapy technology for several other tumors, a Cedars-Sinai Medical Center study here achieved a response with four of seven glioblastoma multiforme patients in a phase-1 trial.

After three intradermal vaccinations with a vaccine made of peripheral-blood dendritic cells pulsed to peptides derived from the surface of each patient's own resected tumor, the four responders all showed enhanced cytotoxic T-cell activity, Dr. Keith L. Black and colleagues reported in the February *Cancer Research*. "The results greatly exceeded our expectations," Dr. Black said.

Autologous dendritic-cell vaccines have also been tried in other centers for lymphoma, melanoma, prostate cancer, and renal-cell carcinoma.

The researchers said that the dendritic cells help induce a cytotoxic T-cell response by acting as an antigen presenter for the glioblastoma cells, known to be poor antigen presenters.

Median survival for the seven was 455 days, compared with 257 days for 42 controls given standard therapy. There was also T-cell activity at the site of the tumor in two of four patients who had subsequent surgery for tumor progression. This "demonstrated that dendritic-cell vaccination can induce intraglioma T-cell infiltration despite the immunologically privileged status of the central nervous system," the investigators said.

The vaccines were given at two-week intervals. Systemic T-cell activity was tested a week after each vaccination, and six and 12 weeks after the last vaccination. T-cell activity was still evident in the four responders after 12 weeks.

There were no serious side effects. One patient had a mild fever and developed nausea and vomiting several weeks later. Another patient had palpable lymph nodes.

## Carcinogenesis: An Animal Hypothesis

**HEIDELBERG, Germany**—A researcher here has floated a provocative theory that the genesis of many malignancies may be animal viruses encountered via food, work, or pets.

Dr. Harald zur Hausen of Deutsches Krebsforschungszentrum reasons that because bench studies have shown that there are several types of human viruses that have oncogenic potential in animals, the reverse could be true.

But he concedes that though animal-human transmission of oncogenic viruses has been shown experimentally, it's not clear it could happen under natural conditions.

Human exposure to these viruses is most likely to occur through diet—the handling and consumption of meat, eggs, and dairy products, he wrote in a feature in the Feb. 3 *Lancet* titled "Hypothesis."

He said that butchers, meat cutters, dairy workers, and veterinarians may be vulnerable, and that household pets such as dogs, cats, rabbits, guinea pigs, and birds may be vectors.

Dr. zur Hausen believes that human tumors should be systematically assessed for nonhuman viruses.

## Exercise a Plus in Breast-Cancer Therapy

These findings did not vary irrespective of whether women were given chemotherapy, hormonal treatments, or radiation. But exercisers who took tamoxifen, which may trigger weight gain, were the most likely to lose weight, an average of two to eight pounds.

"Breast-cancer patients receiving adjuvant therapy, including chemotherapy, are willing, and quite capable, of participating in exercise," said Dr. Segal. "Even moderate physical activity was meaningful, resulting in an increased ability to function and feel independent."

## Breast-Cancer Metastasis Is Tied To Tumor Lymphangiogenesis

**BOSTON**—A vascular endothelial growth factor may be intimately involved in breast-cancer metastasis via lymphangiogenesis.

Using human breast tumors transplanted onto the mammary fatpads of nude mice, a Harvard-led international team has found strong evidence that not only does lymphangiogenesis occur in breast lesions but that VEGF-C is a molecular causal link to metastasis.

Breast tumors in the mice that were made to overexpress VEGF-C created a system of lymphatic vessels through which malignant cells exited the tumor, Dr. Michael Detmar of Mass General and colleagues reported in the February *Nature Medicine*. Conventional wisdom has held that the pressure is too great inside a tumor to allow the presence of lymph vessels.

The researchers made their observations with a new imaging technique involving the lymphatic-vessel marker LYVE-1. Expression of VEGF-D, which is structurally related to VEGF-C, was undetectable.

The number of vessels in the tumor correlated with the number of metastatic cells found in regional lymph nodes and lungs, they reported.

The researchers believe that the density of lymph vessels in a tumor could allow clinicians to predict the risk of metastases. Blocking VEGF-C is an avenue that should be explored to prevent metastases, they added.

In an accompanying commentary, Dr. Karl H. Plate of FAU Erlangen-Nurnberg in Germany predicted that lymphangiogenesis will become a new focal point of cancer research.

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## A Carotid Stent Relieves ‘Hostile-Neck’ Stenosis

**PARIS**—The increasingly ubiquitous arterial stent may turn out to be a remedy for head-and-neck cancer patients’ radiation-induced carotid stenosis.

In a study at the Hopital Lariboisiere here, neuroradiologists did angioplasty on stenoses in the carotid artery of seven head-and-neck cancer patients, six with neurological symptoms, and inserted a self-expandable stent. There was a total of 10 arteries stented in nine procedures, with no serious complications.

After an average follow-up of eight months (range, 3 to 24 months), all patients were symptom-free, and Doppler ultrasound showed no restenoses, Dr. Emmanuel Houdart and colleagues reported in the January *Stroke*. Radiation-induced stenosis, often diffuse, occurs in about 12% of patients who have head-and-neck radiation, the fibrosis complicating endarterectomy.

Though the report concluded that the carotid stents seemed attractive for “hostile-neck” patients, it cautioned that stenting for head-and-neck cancer patients had yet to be compared directly with endarterectomy for routine arterial lesions.

## Cancer-Screening Decisions Seen as Unilateral Dictates

**NEW YORK**—Some primary-care physicians don’t even give patients a chance to say yes or no to cancer screening.

A questionnaire sent to primary-care attendings, residents, and interns at three New York hospitals has reinforced public-health concern that physicians often provide or withhold cancer screening without involving patients in the decision-making process.

The physicians reported they make peremptory decisions on the basis of their own biases, because of a lack of time, a concern over the “complexity of the topic,” language barriers, or their belief that a discussion with a patient would inevitably lead to the decision they had in mind in the first place.

The survey of 86 attendings and 83 house staffers found that only 17% would base their decision to screen on patient preference, Dr. Andrew Dunn of Mount Sinai here and colleagues reported in the February *American Journal of Preventive Medicine*.

Depending on the scenario, 16% to 34% of the physicians would not discuss the risks and benefits of mammography or PSA screening with a hypothetical 45-year-old woman, 55-year-old woman, or 55-year-old man. About a quarter of the physicians indicated that they wouldn’t have discussions with patients because they feel the talk wouldn’t influence whether they ordered the test.

But 84% of the attendings and 78% of the house staff said they’d definitely or probably discuss the risks and benefits of screening with the 45-year-old woman.

Seventy-five percent of the attendings and 69% of the house staff would talk about mammography with the 55-year-old woman, and 69% percent of the attendings and 66% of the house staff would discuss PSA screening with the hypothetical male patient.

## IG: Medicare Pays \$1 Billion Too Much for Drugs

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underpayment for drug administration. HCFA has conceded that practice expenses for drug administration need to be reevaluated.

And Congress on the final day of the last session ordered HCFA to freeze the redefinition of the average wholesale price for all Part B covered drugs until Sept. 1 so that the General Accounting Office can study drug pricing and practice expense payments.

## Four okay, one to go

**Computerized Thermal Imaging** of Layton, Utah, said it received a letter of acceptance from the FDA for Module 4 for its Computerized Thermal Imaging System as an adjunct to mammography and clinical breast exams. The system uses a heat-sensitive camera to record thermal images of breast tissue. The company said it will submit the fifth and final module for FDA consideration this year.

## TheraFab for lung cancer

**Antisoma** of London said it has begun a phase-1 trial of TheraFab for small-cell lung cancer. The injectable radiolabeled antibody fragment will be given in combination with external-beam radiotherapy to 20 patients in Australia and Europe.

## Canadians okay doxorubicin liposome

**Alza** of Mountain View, Calif., announced that Caelyx (pegylated liposomal doxorubicin) has been approved in Canada for advanced ovarian cancer in women who have failed first-line platinum-based therapy. The agent is marketed in the U.S. as Doxil and has been FDA-approved since June 1999 for metastatic ovarian cancer in women whose disease is refractory to paclitaxel- and platinum-based chemotherapy.

## New vistas for arsenic

**Cell Therapeutics** of Seattle is starting two phase-2 trials of Trisenox (arsenic trioxide) for recurrent or refractory multiple myeloma. The first will evaluate the agent in 55 patients who have relapsed following up to three treatments. The other study, evaluating Trisenox with high-dose steroids, will enroll 55 patients who have not responded to first-line treatment. Trisenox is FDA-approved for acute promyelocytic leukemia.