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FEATURES DESK

## Cancer doctors share new findings

BY THOMAS H. MAUGH II

**Among the topics: An experimental blood test might boost accuracy of prostate screenings.**

Hope for a better prostate cancer test, potential new uses for a largely discredited lung cancer drug and a warning for breast cancer patients all emerged last week from a meeting of the American Society of Clinical Oncology in Orlando.

Prostate cancer is the most common form of cancer in American men, with an estimated 186,320 cases diagnosed last year. But every year, at least that many men undergo painful and expensive prostate biopsies after routine screening has revealed high levels of prostate-specific antigen, or PSA, and yet the men turn out to not have tumors.

Many critics have argued that the large number of unnecessary biopsies grossly limits the benefits of the PSA test and have called for a halt to its use.

An experimental blood test that looks at the activity of six genes linked to prostate tumors could greatly improve the accuracy of PSA testing and "could spare tens of thousands of men from undergoing prostate biopsy each year" if validated in further studies, Dr. Robert W. Ross of Harvard Medical School's Dana-Farber Cancer Institute in Boston told researchers.

Together, the two tests detect cancer accurately more than 90% of the time, compared with only about 60% to 70% for the PSA test alone, Ross said. Widespread use could spare men anxiety and needless testing, he said, and could save the U.S. health-care system more than \$2 billion per year.

Ross and Dr. William K. Oh of Dana-Farber worked with researchers at Source MDx in Boulder, Colo., to develop the test, which examines signs of tumor gene activity (RNA) in the blood.

The team examined 174 genes associated with inflammation and cancer, studying 76 men with known prostate tumors and 76 healthy men. They found that six genes were closely associated with the presence of a tumor. RNA from five of the genes was found at lower levels in the blood of men with prostate tumors, while that from the sixth gene was found at higher levels.

The scientists put the test through its paces in a two-year study of 204 men with known prostate cancer, 110 men with benign prostatic hyperplasia

(a harmless enlargement of the prostate that is responsible for many false positives on the PSA test) and 170 healthy men.

When used alone, the six-gene test detected about 86% of prostate tumors and had a specificity of 83% -- meaning that 17% scored as positive even though they didn't have a tumor. But when it was combined with the PSA test, the two detected 87% of tumors and the specificity was more than 91% -- only 9% of the positive scores were in error.

The researchers and the company are organizing a clinical trial of the test with 1,000 men, to begin this year. Karl Wassman, chief executive of Source MDx, said the new test will probably cost "a couple of hundred dollars," much less than the \$2,000 cost for a biopsy.

The study was funded by Source, Dana-Farber and private donors.

Lung cancer drug

A cancer drug once regarded as a flop may reemerge as an effective drug in some populations, Japanese researchers reported.

Gefitinib -- marketed as Iressa by AstraZeneca -- was approved in 2002 as a treatment for small-cell lung cancer, the most common form of the disease, but subsequent large studies failed to prove its efficacy. Oncologists noticed, however, that it apparently provided benefit for some Asians, nonsmokers with a mutation in a gene that serves as the blueprint for a protein called EGFR. About 10% of lung cancer patients carry the mutation.

In a new study, Dr. Masahiro Fukuoka of the Kinki University School of Medicine in Osaka studied 261 cancer patients with mutations in the EGFR gene and 176 patients without the mutation. Half in each group received gefitinib and half received a standard chemotherapy combination.

In the patients with the gene mutation, those receiving gefitinib went for a median of 9.5 months before the tumor resumed growing, while those receiving conventional chemotherapy went just 6.3 months. In those without the mutation, the situation was reversed: Those receiving conventional chemotherapy went a median of 5.5 months before tumors resumed growing; those receiving gefitinib went 1.5 months.

The study was funded by AstraZeneca.

Antidepressant risk

A diagnosis of breast cancer can lead to

depression, but some antidepressants used with the chemotherapy drug tamoxifen can double the risk of the cancer returning.

Tamoxifen, which interferes with the production of estrogen needed by many tumors, has been used for more than 30 years to prevent tumor recurrence in breast cancer patients and for 10 years to prevent breast cancer in women at high risk. Antidepressants are also frequently prescribed, not just for depression but to limit the hot flashes that estrogen deprivation can cause.

Tamoxifen is activated inside the body by a liver enzyme called CYP2D6. Some antidepressants, such as Paxil, Prozac and Zoloft, are moderate-to-potent inhibitors of this enzyme. Others, such as Celexa, Lexapro and Luvox, are weaker inhibitors. Laboratory studies have suggested the potential for harmful interactions between all of these antidepressants, known as selective-serotonin reuptake inhibitors, and tamoxifen.

Researchers at Medco Health Solutions Inc., a pharmacy benefits company in Franklin Lakes, N.J., searched their medical and drug records of more than 10.7 million people to identify women who were taking one or both drugs. They found 945 women taking tamoxifen and 353 taking tamoxifen and an SSRI.

Dr. Robert Epstein, the chief medical officer at Medco, told the ASCO meeting that women taking Paxil, Prozac or Zoloft in combination with tamoxifen had a 16% risk of breast cancer recurrence compared with a 7.5% risk among those taking tamoxifen alone. Those taking other antidepressants in the same family had a 14% risk of recurrence.

In an e-mailed statement Tuesday, Food and Drug Administration spokeswoman Karen Riley said that the agency is likely to revise the tamoxifen label to warn women and doctors against using SSRIs in conjunction with it. Epstein said his company is also notifying doctors. Some doctors have already switched patients who need an antidepressant to Effexor, which seems to be less harmful.

About 187,000 American women are diagnosed with breast cancer each year and 41,000 die from it. The study was financed by Medco.

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