FDA approves genetic test for women with breast cancer

Deborah Josefson, *San Francisco*

The Food and Drug Administration in the United States has recently approved a gene based test that may help to predict the recurrence of breast cancer. The test detects levels of Her2/neu, a gene on chromosome 17 which is amplified in a subset of breast cancers.

The test will be manufactured by Oncor under the name Inform and is expected to be commercially available for a cost of about \$200 (£125) within three months. This is the first time a gene based test for cancer has been approved by the Food

and Drug Administration. The predictive value of the test, however, is controversial.

About 180 000 women in the United States are diagnosed with breast cancer annually, and 44 000 die of the disease each year. Two thirds of women with breast cancer have localised disease at the time of diagnosis, and 40 000 a year experience a recurrence despite surgical resection. Women whose lymph nodes are positive for metastatic disease at the time of diagnosis routinely undergo chemotherapy, with or without ancillary

treatment with antioestrogens or radiation treatment. Therapeutic decisions for patients with node negative disease are more difficult, and increasingly doctors and patients are turning to molecular markers to help them navigate among the choices.

Many studies have shown that the Her2/neu gene is amplified in a subset of breast cancers and some have implicated it in metastatic disease. About a third of breast cancers test positive for amplification of the Her2/neu gene.

In clinical trials sponsored by Oncor 31% of patients with localised breast cancer at the time of diagnosis who had a positive Her2/neu test died within five years of surgery, whereas 97% of those with a negative test were still alive five years after surgical resection of the tumour. Dr Jeffrey Ross, chairman of pathology at the Albany Medical Center, and a participant in Oncor's studies, said: "The amplification of the Her2/neu gene predicted which women would have a higher risk of relapse and which women were more likely to die of the disease. The Her2/neu test is designed to provide additional information to the patient and her oncologist."

But some are cautious about using the test. Daniel Hayes, chief of breast oncology at Lombardi Cancer Center, said: "I think it is dangerous to use Her2 to make clinical decisions because I don't think we know what we are doing with it."

The American Society of Clinical Oncology recently voted against recommending the test for patients with breast cancer because of uncertainty about what to do with the results. Numerous research studies have shown that amplification of Her2/neu does correlate with both earlier relapse and shorter survival in women with node positive breast cancer, but in node negative cancers the prognostic significance is much less clear. It is precisely in the node negative population, however, that the test would be most useful.

The spokesman for the Food and Drug Administration, Dr Steve Gutman, said: "This is an interesting and exciting new test, but it should not be used alone in making treatment decisions in patients with breast cancer." The administration also cautioned that the current test has a high false positive rate but is quite accurate in assuring a woman that her tumour is Her2/neu negative.

Oncor's chief executive, Stephen Turner, said that the next step is studying whether the Inform test can help to improve breast cancer survival by helping to risk stratify women into different therapies.

In a related development many medical research centres have already started clinical trials of monoclonal antibodies directed against the Her2/neu gene product in women whose breast cancers carry the amplification. □

A third of breast cancers carry the Her2/neu gene amplification

US NATIONAL CANCER INSTITUTE/SPIL

Warning about contraceptive device given

Susan Mayor, *London*

The Department of Health has advised GPs that the contraceptive device Persona may be unsuitable for couples who would find an unplanned pregnancy completely unacceptable. Persona tests hormone levels in urine to enable women to avoid unprotected intercourse during the fertile phase of the menstrual cycle.

The warning came after the Medical Devices Agency carried out an investigation into Persona

in response to complaints about its reliability from users, GPs, and trading standards officers. The manufacturers of the device, Unipath, claim that a clinical trial conducted before the device was marketed showed that it is 94% reliable, which means that if 100 women use Persona for one year six would be expected to become pregnant as a result of the device incorrectly identifying the fertile phase.

The Medical Devices Agency stated that it was unable to substantiate the reliability because Unipath declined to provide data from the trial. However, John Newton, professor of obstetrics and gynaecology at the University of Birmingham and one of the independent experts who took part in the investigation, said:

"The clinical data are available—the Medical Devices Agency sent them to me. I am very happy with the results, which were collected carefully following good clinical guidelines. The device is 94% reliable."

Last week's letter from the agency to GPs suggested that Persona is a useful addition to the range of contraceptive choice. But it warned: "Persona is basically a test-based form of the rhythm method of contraception. However, due to its technological basis, expectation of Persona may be higher than for other forms of contraception."

The agency said: "Users of Persona should be aware that 94% reliability as defined may also be expressed as a risk of 1 in 17 users becoming pregnant per

year of use." The agency also pointed out that the device is not suitable for women whose menstrual cycle lengths do not fall within the range of 23-35 days; for those using the contraceptive pill, hormone replacement therapy, or infertility treatment; or for those who have recently given birth or are breast feeding.

Dr Keith May, vice president for research and development with Unipath, confirmed that its clinical trial carried out before the launch had included women from a wide range of ages, educational background, and social status. "We have tried right from the start to give all of the information necessary for consumers to make informed decisions, and we continue to work to improve our communication with users." □