NEWS

EXPERIMENTAL PROGNOSTIC TEST IDENTIFIES BREAST CANCER PATIENTS AT GREATEST RISK FOR METASTASIS

Objective tool may help patients avoid chemotherapy

An experimental prognostic assay that, at the time of diagnosis, identifies which breast cancer patients are at greatest risk for metastatic disease did so with more than 90% sensitivity, according to a study published in the February 2005 issue of the *Lancet*.

The assay represents the first prognostic molecular marker that could be used with all lymph-node-negative (LNN) breast cancer patients, regardless of age, tumour size and grade, or oestrogen-receptor/progesterone-receptor (ER/PR) status. This diagnostic tool is being developed by Veridex, LLC, a Johnson & Johnson company.

Once the new genomic assay is further developed for commercial use, oncologists could have access to reliable and objective information not previously available with this level of sensitivity to assess individual risk in a broad range of LNN breast cancer patients. Having such knowledge will help physicians and patients to make individual and more effective decisions regarding postsurgical therapy; most notably, the 76-gene signature, on which the assay is based, could help to identify patients who may not require adjuvant chemotherapy or could undertake a less aggressive course of treatment.

'These findings could one day profoundly change treatment standards for lymph-node-negative breast cancer patients by more precisely determining who is at risk of metastasis,' said David Atkins, General Manager, Molecular Diagnostics, Veridex, LLC, and a senior author of the study. 'This purely prognostic tool, which is the only one of its kind that can be used with such a broad range of patients, marks a significant step toward a time when oncologists have the information to make quantitative, objective, effective treatment choices tailored precisely to each patient's unique risk profile.'

The work represented a collaboration between the Erasmus Medical Center-Daniel den Hoed Cancer Center in Rotterdam, the Netherlands, and Veridex, LLC. Researchers analysed tumour samples of 286 breast cancer patients treated during 1980 - 1995, all of whom were LNN and did not receive adjuvant chemotherapy. Importantly, the samples represented patients from routine practice, from all age groups and who were both ER/PR positive and negative.

A genomic signature was constructed using gene expression data of 76 genes derived from extensive tumour gene expression profiling by Veridex, LLC, researchers. This signature showed 93% sensitivity and 48% specificity in a subsequent independent testing set of 171 LNN patients. The gene profile was highly informative in identifying patients who developed metastatic disease within 5 years; it also was a strong prognostic indicator of development of metastases in the subgroups of 84 pre-menopausal and 87 postmenopausal patients, and in patients whose tumours measured 10 - 20 mm, a group for whom prediction of prognosis is especially difficult.

According to John Foekens and Jan Klijn, the study's lead investigators at Erasmus Medical Center, there have been many attempts to find novel markers to identify breast cancer patients at risk for progression, but few have been implemented in routine practice owing to their lack of wide applicability or low prognostic power. Currently available tools are generally restricted to patients with a specific ER status, or to patients already taking tamoxifen.

'These signatures represent a future of hope for improved treatment customisation, but much more research needs to be done before they are made available in routine clinical care,' said Klijn, a medical oncologist.

This prognostic signature was later independently validated in a separate consecutive series of approximately 150 patients from 4 medical institutions. The results were presented at the 2004 San Antonio Breast Cancer Symposium. Although this prognosticator has now been validated in approximately 320 patients, investigators are currently pursuing a further rigorous multi-institution clinical evaluation of the signatures.

About Veridex, LLC

Veridex, LLC, a Johnson & Johnson company, develops cancer diagnostic products that will enable earlier disease detection as well as more accurate staging, monitoring and therapeutic selection. The company is initially developing two complementary product lines: CellSearch (tm) assays that identify, enumerate and characterise circulating tumour cells directly from whole blood; and GeneSearch (tm) assays that use molecular technology to diagnose, stage and more accurately characterise tumours.

For more information, visit **www.veridex.com**
Source: **http://www.jnj.com**

CALCULATION OF MORTALITY IN SOUTH AFRICA CONFIRMS MASSIVE INCREASE IN AIDS DEATHS

A report published in the *AIDS* journal by Medical Research Council and University of Cape Town researchers confirms that there has been a massive increase in AIDS deaths in South Africa (Groenewald *et al.*, *AIDS*, 2005; **19:** 193-201). This yet again demonstrates the need to speed up the implementation

of the Operational Plan for Comprehensive HIV and AIDS, Care, Management and Treatment (published by the Department of Health on 19 November 2003), particularly the rollout of antiretroviral medicine and the mother-to-child transmission prevention programmes.

The Actuarial Society of South Africa estimates that over 300 000 people died of AIDS in South Africa in 2004; the number will rise in 2005 unless many more people receive treatment. Only 20 000 people were receiving treatment in the public sector as of October 2004. This is why the TAC's campaign theme for this year is 'Treat 200 000 People by 2006'.

The rise in AIDS deaths also signals how urgent it is to improve prevention efforts so as to stem unnecessary mortality in the future. Over 1 000 people are estimated to be infected daily in South Africa. A new bold approach to prevention is needed – one that encourages HIV testing and that is much more forthright about the need for condoms to be distributed in schools, places of worship and work. Public messaging must also include people with HIV, sex workers and gay men and not seek to promote interventions or policies that stigmatise people.

Source: TAC Electronic Newsletter, 31 January 2005.

STOP-SMOKING PRODUCTS INCREASE QUIT RATE FOR SMOKERS WHO NEED TO QUIT THE MOST

There is new hope for smokers who are highly dependent on tobacco and who smoke more than two packs per day.

Researchers examined data from two clinical trials and found that a nicotine patch and lozenge marketed by GlaxoSmithKline (GSK) Consumer Health Care can significantly increase the most heavy smokers' chances of quitting successfully.

In the studies, 28.4% of the heaviest smokers using the patch were still not smoking after 6 months, compared with 8.1% using placebo. With the lozenge, 22.1% of the heaviest smokers were still not smoking compared with 6.3% using placebo. The findings were consistent across the two studies reviewed, even though they used different selection criteria, methodology, and cessation treatment methods.

'Nearly ten per cent of smokers smoke more than two packs a day,' said Saul Shiffman, lead author of the study.

Smokers can choose which medicinal nicotine product to use based on their individual smoking habits, including how much they smoke.

Source: **www.gsk.com/**

BHF COMMENTS ON ALCOHOL AND CORONARY HEART DISEASE

New research has suggested that drinking wine could help to keep women's hearts beating healthily.

Scientists studied the effect of alcohol consumption on 102 women under the age of 75 who had survived a heart attack or surgery for blocked arteries.

They found that those who drank a small amount of wine every day for a year had the healthiest heart beat rhythm.

But drinking beer or spirits did not seem to have the same effect, a team from the Karolinska Institute reported.

Commenting on the research, Dr Charmaine Griffiths, BHF spokesperson, said: 'We have known for some time that moderate consumption of alcohol (1 - 2 units per day) might protect against coronary heart disease.

'This research suggests that the type of drink may be important, and adds to the evidence that red wine may have any specific benefits over and above other alcoholic drinks.

'In the short term, the good news is that we can all enjoy alcohol in moderation. However, drinking too much can have an adverse effect on health. It can damage the heart muscle, increase blood pressure and lead to weight gain.

'Wider international research in both men and women is still needed to discover the exact beneficial effects of alcohol on heart health.

'There is no evidence, however, for non-drinkers to start drinking alcohol. Our advice remains the same – the best way to reduce the risk of heart disease is to stop smoking if you smoke, increase levels of physical activity and eat a healthy, balanced diet.'

Note: 1 unit of alcohol = one small glass of wine, half a pint of normal-strength lager or beer or 1 measure of spirits. The BHF statement was issued to BBC Online in response to the study 'Wine drinking is associated with increased heart rate variability in women with coronary heart disease' by Janzky *et al.*, in *Cardiovascular Medicine*, February 2005.

Further information: Jodie Mullish, BHF press office, e-mail: **mullishj@bhf.org.uk**

MILLIONS BEING PUMPED INTO CLINICAL HUMAN TRIALS FOR CORONARY STENT DEVICE

Biotechnology funding organisation, CapeBiotech, has committed R6.7 million to DISA Vascular (Pty) Ltd, a Cape-based medical device company that develops innovative vascular devices for the treatment of heart and peripheral

vascular disease. The allocated funding will be used to develop their drug-eluting stent technology by taking the recently developed Stellium stent through human safety and efficacy trials.

The human study is expected to begin in South Africa later this year and will involve 100 patients.

DISA is presently conducting animal studies in order to obtain ethical approval for the human safety study. Once the Stellium stent has passed the human safety trials, this will pave the way for European Certification, enabling its official launch locally and internationally.

Coronary artery disease is the leading cause of death in the USA, and the cause of more than half of the world's mortality in developed countries. It develops through the build-up of plaque – normally caused by high blood cholesterol levels – along the inner lining of an artery. If the accumulated plaque blocks the whole artery, a heart attack can result.

Treatment for severe coronary artery disease can often be done non-surgically by using stents – tiny metallic tubular mesh-like structures delivered to the heart via a catheter placed in the leg – to re-open blocked arteries. Although stenting is a highly successful treatment, some patients return months later with re-stenosis.

The drug-eluting Stellium stent uses DISA Vascular's ChromoFlex stent platform, made from an exotic cobalt chromium alloy, which has recently been awarded European CE Mark approval.

Dr Greg Starke, CEO, says, 'Our cobalt chromium stent incorporates ultra-thin struts, a very low crossing profile, increased vessel wall support and improved flexibility. We designed it so that it would have significantly better deliverability than the thick-strut stainless steel stents that are still the norm. The positive feedback from our sales in Europe and elsewhere has supported these scientific claims.

'The special cobalt chromium alloy offers numerous advantages over the more conventional stainless steel because of the increased strength and radiographic visibility of the material. There are currently very few CE Marked cobalt chromium stents on the market.'

The Stellium stent combines this new material with a drug so that the active drug is delivered to the target area. DISA Vascular's drug-eluting stent will release a tiny amount of drug from the stent surface to inhibit scar-tissue formation, thereby averting the onset of re-stenosis.

DISA Vascular (Pty) Ltd is a privately owned company in which Bioventures, a South African biotechnology venture capital company, holds a substantial equity position.

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