Chemotherapy and hormonal treatments improve the 15 year survival rate for breast cancer

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Chemotherapy and hormonal therapy achieve long term improvements in survival in women with breast cancer, with even greater increases in 15 year survival than five year survival. These are the latest findings from a five yearly meta-analysis published last week (*Lancet* 2005;365:1687-717).

The Early Breast Cancer Trialists' Collaborative Group coordinated the world's largest collaborative analysis of cancer trials, including data from 145 000 women with early breast cancer who had been studied in 194 randomised trials.

The group assessed the

effects after 10 years and 15 years of a range of breast cancer treatments that were being tested in the 1980s, and have since been widely adopted. These included six months of anthracycline based chemotherapy (anthracycline combined with fluorouracil and cyclophosphamide) and five years of treatment with tamoxifen.

As the analysis was restricted to trials that began by 1995, none included newer treatments such as taxanes, trastuzumab, or modern aromatase inhibitors.

The results showed that treatment with both chemotherapy and hormonal therapy approxi-

mately halved the 15 year risk of death from breast cancer, with the survival curves for women treated with these therapies diverging over time compared with those not given them.

Six months of anthracycline based chemotherapy reduced the annual death rate from breast cancer by about 38% (SE 5) for women aged younger than 50 years at the time of diagnosis and by about 20% (4) for those aged 50-69 years when diagnosed. These reductions in breast cancer mortality were largely irrespective of the use of tamoxifen and of oestrogen receptor status, nodal status, or other tumour characteristics.

Chemotherapy regimens based on anthracycline were significantly more effective than CMF (cyclophosphamide, methotrexate, fluorouracil) chemotherapy.

For women with oestrogen receptor positive breast cancer,

five years of adjuvant tamoxifen reduced the annual breast cancer death rate by 31% (SE 3), largely irrespective of the use of chemotherapy and of age, progesterone receptor status, or other tumour characteristics.

Five years' treatment was significantly more effective than just one to two years of tamoxifen (2P<0.00 001 for recurrence, 2P=0.01 for breast cancer mortality). For oestrogen receptor positive tumours, the cumulative reduction in mortality was more than twice as big at 15 years as at five years after diagnosis.

Professor Sarah Darby, professor of medical statistics at the clinical trial service unit, University of Oxford, said on behalf of the collaborative group: "For middle-aged women with hormone sensitive breast cancer, six months of anthracycline based chemotherapy and five years of tamoxifen halves the long term risk of death from the disease." □

Research suggests thrombolysis is effective for acute ischaemic stroke

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New Canadian research suggests that thrombolysis is a safe and effective treatment for acute ischaemic stroke (*CMAJ* 2005; 172:1307-12).

Researchers assessed the safety and effectiveness of tissue plasminogen activator (alteplase, t-PA) as a routine treatment for acute stroke at 60 centres across Canada.

In Canada, alteplase treatment for stroke was conditionally licensed in 1999. As a condition of approval, a prospective registry to monitor safety was mandated by the federal government. The Canadian alteplase for stroke effectiveness study (CASES) was launched to collect data on outcomes for all patients treated with alteplase in Canada.

The 2.5 year study involved 1135 stroke patients at 27 tertiary care hospitals (10 high volume centres) and 33 community hospitals. Patients were given

alteplase intravenously at a dosage of 0.9 mg/kg body weight. The severity of stroke was high (with a median score of 14 (interquartile range 9-19) on the National Institutes of Health stroke scale). The median age of the patients was 73 (63-80) years. Slightly more men than women were treated. A large majority of patients were white. The median time from onset of stroke to treatment was 155 (130-175) minutes.

Researchers at the University of Calgary's stroke programme analysed the data from CASES and concluded that 36.8% of people treated with alteplase had an excellent clinical outcome (a return to a pre-stroke level of functioning, modified Rankin scale score 0-1). Symptomatic intracranial haemorrhage occurred in 4.6% of the patients (95% confidence interval 3.4% to 6.0%); 75% of these patients died in hospital. An additional 1.3% (0.7% to 2.2%) of patients had hemiorolingual angio-oedema.

The national prospective cohort study found no differences in the rates of excellent outcome or symptomatic intracranial haemorrhage between the high volume and low volume centres or between the tertiary care hospitals and the community hospitals.

"This study was a Canadian effort to show that t-PA was effective, safe and could be used in all

An occupational therapist helps a stroke patient improve his coordination. More than a third of patients in the trial returned to a pre-stroke level of functioning

kinds of communities all across the country," said stroke neurologist Dr Michael Hill, one of the authors of CASES. "These findings are extremely important because we now have definitive evidence that widespread use of t-PA for severe stroke will save lives and help many people return to a completely normal life."

To deliver thrombolysis to people with acute ischaemic stroke the appropriate infrastructure and appropriately trained doctors are needed, pointed out Dr Hill. "You need to have people with expertise in stroke medicine who are able to be on hand to make judgments about who should and who should not

receive t-PA for stroke. That training has not been emphasised in the past. It's something that we have to start doing."

The design, management, data collection, and analysis of the study were funded by a partnership between the Canadian Stroke Consortium, the Canadian Stroke Network, and the Heart and Stroke Foundation of Canada. The study was partly sponsored by Hoffmann-La Roche Canada, which commissioned the study, helped with infrastructure and paid investigators an honorarium of \$100 per patient (£54; €79).

The article is at www.cmaj.ca/cgi/content/full/172/10/1307