Older women who take adjuvant treatment after lumpectomy may not need radiotherapy

David Spurgeon *Quebec*

Results of two studies of breast cancer reported in the *New England Journal of Medicine* last week have prompted the authors of an accompanying editorial to propose that lumpectomy plus tamoxifen but without local irradiation "is a realistic choice" for some women over the age of 70 years.

A re-evaluation of the need for radiotherapy has been made against a changed background since earlier trials, says the editorial. These changes include improved imaging and techniques for locating tumours and the widespread use of adjuvant therapy with drugs such as tamoxifen, which reduces the risk of local recurrence and improves survival.

The first new trial compared local radiotherapy plus tamoxifen with tamoxifen alone in women aged 50 years or older

who had undergone breast conserving surgery for breast cancer (*New England Journal of Medicine* 2004;351:963-70). The rate of local relapse was substantially lower in the radiotherapy plus tamoxifen group (0.6%) than in the tamoxifen alone group (7.7%) (hazard ratio 8.3 (95% confidence interval 3.3 to 21.2; $P<0.004$)).

The rate of axillary relapse differed significantly at five years (2.5% in the tamoxifen group and 0.5% in the group given tamoxifen plus irradiation), although overall survival at five years did not differ significantly between the two groups.

The authors of the editorial, Dr Ian Smith and Dr Gillian Ross of the Royal Marsden Hospital, London, said that these results reinforced findings from another recent trial that the addition of radiotherapy to

lumpectomy and tamoxifen for tumours that are 1 cm in diameter or less reduced the risk of local recurrence.

However, the second study published last week led the editorial writers to reach a different conclusion. In this study women aged 70 years or more who had had early, oestrogen receptor positive breast cancer and who had undergone lumpectomy were randomly assigned to receive local irradiation (*New England Journal of Medicine* 2004;351:971-7). As with the first study, the use of radiotherapy reduced local recurrence at five years (recurrence was 4% in the tamoxifen group and 1% in the combined treatment group ($P<0.001$)).

But that was the only significant difference between the two groups. There were no significant differences in the rates of mastectomy for local recurrence or of distant metastases and no difference in overall survival at five years (87% in the group given tamoxifen plus irradiation and 86% in the tamoxifen only group ($P=0.94$)). The authors say that for women aged 70 or older with early, oestrogen receptor

positive breast cancer, lumpectomy plus tamoxifen but without local irradiation "is a realistic choice."

These results "have important implications concerning the use of medical resources," says the editorial, because such women represent a large subgroup—approximately 40 000—of the women in the United States who develop breast cancer each year. "There are clear advantages in identifying subgroups in a large population of elderly women who do not require radiotherapy after lumpectomy and tamoxifen."

In the first trial, the rate of local relapse among women aged 50 years or more who were treated with tamoxifen alone—even among the subgroup with a good prognosis—rose from 5.9% after five years to 15.2% after eight years.

"For women over 70 years of age, however, this is likely to be less of an issue, since breast cancer in this age group is biologically less aggressive and is associated with a lower risk of local recurrence after breast-conserving surgery and with less time at risk," says the editorial. □

Polypill will not change prevention of heart disease

Susan Mayor *BMJ*

Claims that the "polypill"—a combination of a statin, three antihypertensive drugs, folic acid, and aspirin—will cause a major change in the primary prevention of cardiovascular disease are flawed because they are extrapolated from evidence for the individual components, an epidemiologist claimed last week.

Shah Ebrahim, professor of epidemiology of ageing at the University of Bristol, argued that there was only theoretical evidence for the additive effects of the components of the polypill and that it was unlikely to translate into clinical practice.

Speaking at a debate at the recent European Society of Cardiology's annual meeting in Germany, he also argued that there

was a risk of serious adverse effects that would reduce long term compliance and so reduce the benefits. Finally, he calculated that the cost effectiveness of the polypill was poorer than that of other preventive options.

Professor Ebrahim was commenting on claims made in a series of papers published recently in the *BMJ*, including one that said that the polypill could prevent 88% of ischaemic heart disease events and 80% of strokes (*BMJ* 2003;326:1419-24).

The polypill was designed to reduce four cardiovascular risk factors simultaneously: low density lipoprotein cholesterol concentration, blood pressure, serum homocysteine concentration, and platelet function. Its efficacy was quantified from meta-analyses of the effects of the components. It was argued that a third of people taking this pill from the age of 55 would benefit, gaining an average of about 11 years of life free from an ischaemic heart disease event or stroke.

These claims were unlikely to translate into clinical practice, argued Professor Ebrahim.

"There is only weak evidence of any reduction in benefit of ACE [angiotensin converting enzyme] inhibitor when used with aspirin. The heart protection study predicted a 44% reduction in cardiovascular events if the effects of statin, aspirin, ACE inhibitor, and blocker treatments were additive. However, the overall effect was only a 24% reduction in major events" (*Lancet* 2002;360:7-22).

He pointed out that gains were likely to be even lower in

practice. "Studies consistently show that benefits are less than anticipated when applying treatments in routine practice, due mainly to lack of implementation by health professionals and poor compliance by patients."

He said that the evidence for folic acid was particularly weak.

"Safety is also an important issue, particularly if use of the polypill is being considered for primary prevention in healthy people," Professor Ebrahim said. The original polypill paper predicted that 8% to 15% of people taking the combination would experience adverse effects, largely because of the antihypertensive components. "But statin trials have reported very high levels of side effect symptoms, resulting in discontinuation of treatment," he pointed out.

Looking at the cost effectiveness of interventions for prevention, Professor Ebrahim calculated that the cost of the polypill would be \$2600 (£1460; €2150) per life year gained—higher than for interventions such as lowering blood pressure, exercising, smoking control, or taking aspirin. □