より長期のタモキシフェン療法により乳がん再発リスクが低下する（Abstract＃5）

aTTomスタディ: ER陽性乳がん再発および死亡に関して10年間のタモキシフェン療法は5年間の治療よりも優れている

aTTom study: Ten years of tamoxifen is superior to five in reducing ER-positive breast cancer recurrence and death

第49回American Society of Clinical Oncology年次集会で発表された英国aTTomスタディの結果、ER陽性（ER+）乳がん女性において10年間のタモキシフェンを用いた術後補助療法は、現在の標準的な5年のみのタモキシフェン治療に比べ乳がん遅発性再発および死亡の予防効果が高いことが報告された。タモキシフェンを5年間内服した英国女性（6,953人）がさらに5年間のタモキシフェン治療を継続する群または即中止する群に無作為に割り付けられた。無作為化後10年以上（一部の女性は20年もの長期間）追跡された女性5,000人において、乳がん再発は10年間療法群において5年間療法群よりも少なかった（16.7%対19.3%）。診断後5～9年間の再発率および死亡率は治療群間で差がほとんどなかった。しかしその後（つまり診断10年後以降）、タモキシフェン治療継続群は5年で治療を中止した群に比べ、再発率が25%低く乳がん死亡率が23%低かった。これらの結果は、最近雑誌に掲載された国際スタディATLASを補足し確証するものである。

Full Text

A randomized phase III study presented at the 49th Annual Meeting of the American Society of Clinical Oncology reports that ten years of adjuvant treatment with tamoxifen provides women with estrogen-receptor-positive (ER+) breast cancer greater protection against late recurrence and death from breast cancer than does the current standard of only five years of tamoxifen, according to the British aTTom study. While side effects are also increased with longer tamoxifen use, the researchers conclude that the overall benefits greatly outweigh the risk of continuing therapy. The findings from aTTom, a Phase III randomized study, complement and confirm the results of the recently published international study, ATLAS.

Hundreds of thousands of women worldwide take tamoxifen to prevent cancer recurrence after surgery for early-stage breast cancer. Tamoxifen is only effective in women with hormone-sensitive (ER-positive) tumors and most women start taking tamoxifen immediately after completing their initial surgery or chemotherapy.

Prior studies have shown that 5 years of tamoxifen reduces breast cancer death rates by about a third over a 15-year period following diagnosis. This study shows that 10 years of tamoxifen reduces breast cancer recurrence and death rates by an additional 25 percent, from year 10 onwards, compared to 5 years of tamoxifen therapy. The researchers estimate that, compared to taking no tamoxifen, 10 years of tamoxifen reduces breast cancer death rate by a third in the first 10 years after diagnosis and by half subsequently.

"Five years of adjuvant tamoxifen is already an excellent treatment but we thought that longer treatment might be even better because women with ER-positive breast cancer can have recurrences long after treatment is completed. Until now, though, there have been doubts whether continuing tamoxifen beyond five years is worthwhile," said lead study author Richard G. Gray, M.A., MSc., a professor of medical statistics at the University of Oxford in Oxford, United Kingdom. "This study and its international counterpart ATLAS confirm that there is definitely a survival benefit from longer tamoxifen treatment and many doctors will likely recommend continuing tamoxifen for an extra five years."

Between 1991 and 2005, 6,953 women in the United Kingdom who had been taking tamoxifen for 5 years were randomly assigned to continue treatment with tamoxifen for another 5 years or to stop immediately. The women were contacted yearly to assess treatment compliance, recurrence, hospital admissions and death rates. Compliance was good with about 75 percent of women in the 10-year group continuing to take tamoxifen.

With 5,000 women followed for more than 10 years after randomization, and some as long as 20 years, fewer breast cancer recurrences were seen in the 10-year tamoxifen group than in the 5-year group (16.7 percent vs. 19.3 percent). Longer treatment also reduced the risk of dying from breast cancer. The treatment allocation had little effect on either recurrence rates or death rates during the period 5-9 years after diagnosis. After that, however (i.e., during the second decade after diagnosis), the women who had been allocated to continue tamoxifen treatment had a 25 percent lower recurrence rate and a 23 percent lower breast cancer mortality rate than the women who had been allocated to stop after only 5 years.

"This landmark trial confirms recent findings of the ATLAS trial showing that extending therapy with tamoxifen to 10 years significantly lowers breast cancer recurrences and mortality. These results are therefore practice changing for premenopausal women with hormone receptor positive breast cancer and especially relevant for women who are at high risk of recurrence," said Sylvia Adams, M.D., ASCO spokesperson and breast cancer expert.

Women taking tamoxifen can experience side effects similar to menopausal symptoms, such as night sweats and hot flashes. Rare but serious side effects of tamoxifen include increased risk of endometrial cancer, blood clots and stroke. No excess incidence of stroke was observed with 10 years of tamoxifen therapy, though endometrial cancer risk was higher in this arm. Endometrial cancer is often detected early, when it is usually curable; the researchers estimated that for every endometrial cancer death that occurs as a side effect of long-term tamoxifen, there would be 30 deaths from breast cancer prevented. Therefore, the benefits of continuing tamoxifen to 10 years greatly outweigh the risks, said Professor Gray.

Researchers are planning to follow women in this and the ATLAS study for at least five more years to see if there is additional long-term benefit. A retrospective analysis of combined data from aTTom, ATLAS and three smaller trials will be conducted to determine if there are subgroups of women that benefit the most from longer tamoxifen treatment. Ongoing clinical trials are comparing 5-year and 10-year use of aromatase inhibitors to see if longer use leads to more benefit as has been seen with tamoxifen.

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