MEDICAL ONCOLOGY

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In the BIG 1-98 study the aromatase inhibitor, letrozole, produced statistically significant reductions in disease-free survival and distant recurrence compared with tamoxifen in postmenopausal women with endocrine-responsive early-stage breast cancer. In this trial, patients were randomized to 5 years of monotherapy with either tamoxifen or letrozole or to 2 years of letrozole followed by 3 years of tamoxifen, or tamoxifen for 2 years followed by 3 years of letrozole. Owing to the survival benefit demonstrated for patients in the letrozole arm, the tamoxifen arm was unblinded to allow patients to receive letrozole. Of the 2,459 patients enrolled in the tamoxifen monotherapy arm, 619 (25%) selected to crossover to receive letrozole. This selective crossover could lead to an underestimation of the benefit for letrozole, so Colleoni *et al.* investigated whether letrozole monotherapy could prolong overall survival.

The researchers used inverse probability of censoring weighted modeling to confirmed the previous results of a benefit for letrozole and in addition showed a statistically significant improvement in overall survival for letrozole, with an 18% reduction in the risk of death. Moreover, disease-free survival and distant recurrence were also significantly reduced in patients receiving letrozole compared with tamoxifen. These results show a greater benefit for letrozole than anticipated from corresponding risk estimates from intention-to-treat analysis, supporting the up-front adjuvant use of letrozole.

The researchers conclude, “the results of this study indicate that adjuvant treatment with letrozole, compared with tamoxifen, significantly reduces the risk of death in postmenopausal women with hormone receptor-positive breast cancer.”

Lisa Hutchinson

Original article Colleoni, M. *et al.* Analysis adjusting for selective crossover show improved overall survival with adjuvant letrozole compared with tamoxifen in the BIG 1-98 study. *J. Clin. Oncol.* doi:10.1200/JCO.2010.31.6455