アロマターゼ阻害薬は閉経前乳がん患者において有効である（Abstract: LBA1）

ホルモン感受性早期乳がんにおいて術後補助療法にエキセメスタンと卵巣機能抑制とを組み合わせるとタモキシフェンよりも有効である

Adjuvant exemestane beats tamoxifen when combined with ovarian function suppression in hormone-sensitive, early-stage breast cancer

アロマターゼ阻害薬エキセメスタンは、閉経前ホルモン受容体陽性早期乳がん患者において卵巣機能抑制（OFS）と併用することによりタモキシフェンより乳がん再発予防効果が高い、と2014年American Society of Clinical Oncology学会で発表された。TEXTおよびSOFTトライアルの共同解析では、4,690人の女性（平均年齢43歳）をエキセメスタンとOFSの併用またはタモキシフェンとOFSの併用を5年間施行する群にランダムに割り付けた。OFSは薬剤triptorelin、卵巣摘出術、または卵巣放射線照射により行った。一部の患者はまた、主治医の判断で術後化学療法も施行された。5年無がん生存率はエキセメスタンとOFS併用群の91.1%に対し、タモキシフェンとOFS併用群では87.3%であった（28%の相対リスク低下）。エキセメスタンとOFS併用群におけるタモキシフェンとOFS併用群に対する相対リスク低下は、乳がん再発に関しては34%であり、転移リスクに関しては22%であった。5年全生存率は両群ともに高かった—エキセメスタンとOFS併用群95.9%、タモキシフェンとOFS併用群96.9%。このスタディの結果は、*New England Journal of Medicine* オンライン版に同時に掲載された。

Full Text

The aromatase inhibitor exemestane more effectively prevents breast cancer recurrences than tamoxifen, when given with ovarian function suppression (OFS), in premenopausal women with hormone receptor-positive, early breast cancer according a Late Breaking Clinical Trial presentation session at the 50th Annual Meeting of the American Society of Clinical Oncology.

The landmark study was a joint analysis of two-phase III trials, TEXT and SOFT. In the study, exemestane plus OFS reduced the relative risk of women developing a subsequent invasive cancer by 28 percent, and specifically reduced the relative risk of breast cancer recurrence by 34 percent, compared with tamoxifen plus OFS.

"For years, tamoxifen has been the standard hormone therapy for preventing breast cancer recurrences in young women with hormone-sensitive disease. These results confirm that exemestane with ovarian function suppression constitutes a valid alternative," said lead study author Olivia Pagani, M.D., clinical director of the Breast Unit at the Oncology Institute of Southern Switzerland in Bellinzona, Switzerland. "Our findings indicate that exemestane is better than tamoxifen, when given with ovarian function suppression, but longer follow up of these young women will be important to assess survival, and any long-term side effects and fertility."

The TEXT and SOFT trials were led by the International Breast Cancer Study Group (IBCSG) in collaboration with the Breast International Group (BIG) and the North American Breast Cancer Group (NABCG) as a successful, worldwide collaboration spanning 27 countries and six continents.

The joint analysis of TEXT and SOFT is the largest study worldwide evaluating adjuvant aromatase inhibitor therapy with OFS in young women with breast cancer, and the first to demonstrate the value of such therapy in women with hormone receptor-positive cancer. Aromatase inhibitors have primarily been used in postmenopausal women, because their use requires that women have a low level of estrogen. In the TEXT and SOFT trials, ovarian function suppression was used in premenopausal women to emulate the low estrogen levels that naturally occur in menopause.

The standard adjuvant endocrine therapy for premenopausal women is currently five years of tamoxifen. In some countries, physicians recommend adding OFS to tamoxifen in high-risk younger women. The SOFT trial also addresses the impact of adding OFS to tamoxifen, and the results will be available in late 2014. The joint analysis of the TEXT and SOFT trials studied the outcomes of 4,690 women, whose average age was 43 years, who were randomized to receive exemestane plus OFS or tamoxifen plus OFS for five years. OFS was achieved through treatment with the drug triptorelin, surgical oophorectomy, or ovarian irradiation. Some women also received adjuvant chemotherapy, as decided with their physician.

The cancer-free survival at five years was 91.1 percent in the exemestane plus OFS group, versus 87.3 percent in the tamoxifen plus OFS group, which was a 28 percent relative reduction in risk. There was a 34 percent relative reduction in breast cancer recurrence risk in the exemestane plus OFS group compared to the tamoxifen plus OFS group and a 22 percent relative reduction in metastasis risk. The five-year overall survival rates were high in both groups — 95.9 percent in the exemestane plus OFS group and 96.9 percent in the tamoxifen plus OFS group. Longer follow-up is needed to accurately assess the impact of the two treatments on long-term survival.

The side effects were similar to those reported in previous studies comparing adjuvant aromatase inhibitors and tamoxifen in postmenopausal women, and differed depending on the agent. Despite the side effects, only 14 percent of TEXT and SOFT participants completely stopped the protocol-assigned treatments early – an adherence rate that is higher than what is seen in everyday practice. Dr. Pagani stated that this high compliance rate is important information for doctors who wish to propose this treatment to their patients.

The TEXT and SOFT trials were conducted at the same time and in the same general population – premenopausal women with hormone receptor-positive early breast cancer. The original plan was to analyze each trial separately as well as jointly, given the common treatment groups of exemestane plus OFS and tamoxifen plus OFS in both trials. However, by combining the trials in a joint analysis, the results could be presented earlier, giving physicians and patients the possible benefit of acting on the results sooner.

ASCO Perspective: "Young women with breast cancer have long needed additional treatment options after surgery, and now they may have one," said ASCO president Clifford A. Hudis, M.D., FACP. "Tamoxifen has been a gold standard for decades and has significant benefits. Now, with ovarian suppression, aromatase inhibitors are an option offering a further reduction in the risk of recurrence."

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