



TEN BEST READINGS RELATING TO BREAST CANCER

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The 10 best recent articles in the medical literature relating to breast cancer are reviewed here.

Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. *N Engl J Med.* 2001;344:783-792.

This is the key clinical work that first demonstrated the clinical benefit and prolongation of survival from the addition of trastuzumab to chemotherapy in patients with metastatic breast cancer that overexpresses HER2.

Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomized trial. *Lancet.* 2002;359:2131-2139.

Anastrozole is an effective and well-tolerated adjuvant endocrine option for the treatment of postmenopausal patients with hormone-sensitive early breast cancer. Longer follow-up is required before a final benefit:risk assessment is made.

Grady D, Herrington D, Bittner V, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). *JAMA.* 2002;288:49-57.

Hulley S, Furberg C, Barrett-Connor E, et al. Noncardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/Progestin Replacement Study follow-up (HERS II). *JAMA.* 2002;288:58-66.

Women have been taking estrogen replacement therapy despite a long-suspected increased

risk of breast cancer. The primary reason for prescribing HRT was that the intervention was believed to benefit the heart and the bones. These two well-performed studies show that that these benefits are minimal at best and not worthwhile, considering the increased risk for breast cancer. These studies are important in that only prospective studies can overcome long-held beliefs.

Kauff ND, Satagopan JM, Robson ME, et al. Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med.* 2002;346:1609-1615.

This review of outcomes in 170 women suggests that salpingo-oophorectomy in carriers of BRCA mutations can decrease the risk of breast cancer and BRCA-related gynecologic cancer.

Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumors. *Nature.* 2000;406:747-752.

Gene expression patterns using complementary DNA microarrays allow classification of tumors distinguished by pervasive differences in their gene expression patterns. These techniques will become clinically useful in the near future.

Cox CE, Nguyen K, Gray RJ, et al. Importance of lymphatic mapping in ductal carcinoma in situ (DCIS): why map DCIS? *Am Surg.* 2001;67:513-521.

This study challenges the credo of avoiding axillary node sampling in patients with DCIS. Three hundred forty-one patients

presented with a biopsy diagnosis of DCIS or DCISM with microinvasion. Two hundred forty (70%) underwent sentinel node biopsy at their definitive procedure. Of 224 patients with a biopsy diagnosis of DCIS, 23 (10%) were upstaged to infiltrating ductal carcinoma (IDC) at their definitive therapy; of 16 patients with a biopsy diagnosis of DCISM, 7 (44%) were upstaged to IDC. Lymph node metastases were detected in 26 (13%) of 195 patients with a definitive diagnosis of DCIS, in 3 (20%) of 15 patients with a definitive diagnosis of DCISM, and in 8 (27%) of 30 with a definitive diagnosis of IDC.

Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;347:1233-1241.

Lumpectomy followed by breast irradiation continues to be appropriate therapy for women with breast cancer, provided that the margins of resected specimens are free of tumor and an acceptable cosmetic result can be obtained.

Shang Y, Brown M. Molecular determinants for the tissue specificity of SERMs. *Science.* 2002;295:2465-2468.

Both tamoxifen and raloxifene induce the recruitment of corepressors to target gene promoters in mammary cells. In endometrial cells, tamoxifen, but not raloxifene, acts like estrogen by stimulating the recruitment of coactivators to a subset of genes. The estrogen-like

activity of tamoxifen in the uterus requires a high level of steroid receptor coactivator 1 (SRC-1) expression. Thus, cell type- and promoter-specific differences in coregulator recruitment determine the cellular response to SERMs.

First results from the International Breast Cancer Intervention Study (IBIS-I): a randomized prevention trial. *Lancet.* 2002;360:817-824.

This tamoxifen-breast cancer prevention trial recruited 7,152 women. After 50 months median follow-up, prophylactic tamoxifen was shown to reduce the risk of breast cancer by approximately one third. The overall risk to benefit ratio for the use of tamoxifen in prevention, however, is still unclear.

Meijers-Heijboer H, van den Ouweland A, Klijn J, et al. Low-penetrance susceptibility to breast cancer due to CHEK2(*)1100delC in non-carriers of BRCA1 or BRCA2 mutations. *Nat Genet.* 2002;31:55-59.

The search for genes associated with increase familial risk for breast and ovarian cancer continues. Mutations in BRCA1 and BRCA2 account for only a small fraction of breast cancer susceptibility. CHEK2 (also known as CHK2) encodes a cell-cycle checkpoint kinase implicated in DNA repair processes involving BRCA1 and p53. This variant is present in 5.1% of individuals from families with male breast cancer. The authors estimate that the CHEK2 (*) 1100delC variant results in an approximately twofold increase of breast cancer risk in women and a tenfold increase of risk in men.