Bone Metastases in Women With Procollagen Peptide May Predict Long-Term Treatment

Researchers from the United Kingdom and Finland presented the results from a study comparing bone marrow density and serum biochemical markers of bone turnover where bone-specific alkaline phosphatase, carboxy-terminal telopeptide of type I collagen, and N-terminal procollagen peptide of type I collagen (PINP) were analyzed at one and two years. A total of 498 women with breast cancer were entered in the trial and received either clodronate (a bisphosphonate that reduces osteoclast activity) or a placebo (n = 255). Bone marrow density was measured by dual x-ray absorptiometry at trial entry and annually. The researchers found a significant correlation between oral clodronate and an increase in mean bone marrow density in the spine and hip after two years. This increase was associated with a significant decrease in serum PINP. Patients in the control placebo group demonstrated a significant decrease in bone marrow density in the spine and hip after two years. 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**Microarrays May Predict Docetaxel Responders and Nonresponders**

Taxotere® (docetaxel, Aventis Pharmaceuticals, Bridgewater, NJ) is an important agent used in adjuvant chemotherapy. Although Taxotere appears to induce one of the highest chemotherapy response rates in patients with breast cancer, tumor resistance is frequent. Researchers from Baylor College of Medicine in Houston, TX, examined tumor samples from 24 patients who received 12 weeks of Taxotere therapy in an effort to quantify gene expression patterns in responders and nonresponders. These patients represented the extremes of treatment success or failure. Microarray technologies and DNA chip analyzer software were used to determine expression patterns for 12,000 genes; of these, 747 were selected for comparison purposes. Statistical tests allowed identification of a subset of 100 genes that predict the likelihood of response to Taxotere. The researchers found that nonresponders had elevated levels of microtubule components and responders had elevated levels of genes associated with stress (i.e., microfilament, immune response, inflammatory response, heat shock, and mitochondrial genes). The researchers concluded that cDNA array-based tumor profiles may be used to predict responses to single-agent Taxotere therapy. As a result, this could reduce unnecessary treatment, toxicity, and cost to women with breast cancer.

**Gene Expression May Predict Postoperative Prognosis for Patients With Breast Cancer**

The absence of estrogen receptors (ERs) in breast tumors is associated with poor prognosis. Researchers from the Nippon Medical School in Kawasaki, Japan, and the Cancer Institute in Tokyo, Japan, presented the results of a study aimed at identifying prognostic indicators for patients with ER-negative breast tumors. They used microarray technologies to examine breast tissues from patients who survived five years and from those who did not. Total RNA was extracted from normal and tumor breast tissues and then amplified and labeled. A total of 25,344 genes were examined by competitive hybridization on glass slides. Results were confirmed by reverse transcriptase polymerase chain reaction. Gene expression was found to be significantly different for several genes in the two patient groups. The researchers suggested that genes in each group might serve as new genetic prognostic markers.

**Additional Research Highlights**

**Short Interval Follow-Up for Probably Benign Mammogram Findings May Be Unnecessary**

A 2003 article in the *Journal of the National Cancer Institute* (Vol. 95, No. 6, pp. 429–436) examined the predictive value of a “probably benign finding” in mammogram screenings. The researchers carried out a longitudinal analysis of a prospective cohort of 68,126 postmenopausal women (50–79 years old) from the Women’s Health Initiative at 40 centers in the United States. Participants had mammograms at baseline and annually for at least two years. Of the eligible women, 5% (n = 2,927 of 58,408) were given recommendations for short-interval follow-up. The incidence of breast cancer for these women was 1% at two years compared to 0.6% and 0.5% for women who had baseline benign or negative findings. The researchers concluded that a recommendation for short-interval follow-up had a low-positive predictive value for breast cancer among postmenopausal women during the two-year follow-up. They suggested that a recommendation of repeat mammography in six months for “probably benign” findings should be reconsidered.

**Levetiracetam Provides Pain Relief and Reduces Need for Opioids in Patients With Neoplastic Pain**

Researchers from the A&A Pain Institute in St. Louis, MO, presented the results of a study of levetiracetam (LEV), an antiepileptic agent, for pain relief at the Annual Meetings of the American Pain Society from March 20–23, 2003, in Chicago, IL. Their study involved six participants with neoplasms: four with neoplasms invading the brachial plexus and two whose neoplasms were in the lumbosacral plexus. Initially, the patients reported severe pain (8–9 out of 10 on a visual analog scale [VAS]). Pain was severe despite the use of parenteral opioids and other pain therapies. Participants received oral LEV titrated for up to two weeks for maximum doses of 500–1,500 mg twice a day. Both VAS and opioid use were recorded. The results showed that VAS scores were reduced to 0–3 out of 10 in 3–14 days and opioid use was reduced by 50%. LEV was well tolerated with no adverse effects. The researchers recommended that these results should be confirmed by larger, controlled studies.

**Combination Vinorelbine and Gemcitabine Is Not More Effective Than Either Agent Alone**

The results of a phase III trial in the Multicenter Italian Lung Cancer in the Elderly Study were presented in the *Journal of the National Cancer Institute* (Vol. 95, No. 5, pp. 362–372). The study was an open-label, randomized trial comparing the efficacy and toxicity of vinorelbine or gemcitabine alone or in combination. Participants (N = 698) were aged 70 or older with advanced non-small cell lung cancer (NSCLC) and were assigned randomly to one of three treatment arms: vinorelbine 30 mg/m², gemcitabine 1,200 mg/m², or vinorelbine 25 mg/m² and gemcitabine 100 mg/m². Chemotherapy was given on days one and eight every three weeks for a maximum of six cycles. The combination treatment did not improve survival relative to the two single-agent–treatment arms. Quality-of-life measures were found to be similar across all three treatment groups; however, toxicity was higher for the combination-treatment group. The researchers recommended that single-agent chemotherapy (vinorelbine or gemcitabine) is preferred over combination chemotherapy for palliation treatment in elderly patients with advanced NSCLC.