Advanced Metastatic Disease

Transdermal Fentanyl May Provide Effective Analgesia for Patients With Advanced Metastatic Disease

A study presented by researchers from Siena, Italy, examined pain control using transdermal fentanyl for patients with advanced metastatic disease. Fentanyl is a synthetic opioid that interacts primarily at μ receptors. Twenty patients receiving anticancer treatment were treated with 25-mg/h fentanyl patch. Patients included in the study had a high expectation of remission using specific anticancer treatments and a pain intensity higher than four using a visual analog scale. The pain lasted five days despite continuous use of nonsteroidal anti-inflammatory drugs. The fentanyl treatment lasted two or three months; all patients were living after six months of treatment and experienced an average increase in Karnofsky Performance Status of 20–30 points. Toxicity was classified as mild—nausea and vomiting occurred in three patients, and confusion and delirium occurred in two patients. Two patients developed a paralytic ileus that was treated by hospitalization and rehydration and resolved in three to four days. The researchers concluded that transdermal fentanyl was well tolerated and may be advantageous during chemotherapy or radiotherapy in reducing pain and improving quality of life.

Dexketoprofen Is Effective and Well Tolerated for Bone Pain in Patients With Cancer

A collaborative group of researchers from Spain presented the results of a randomized double-blind study of dexketoprofen trometamol compared to ketorolac for patients with moderate to severe bone cancer pain who had not been previously treated with opioids. The variables used were pain intensity scores (PI) using a visual analog scale and pain rating indices (PRI) at the end of treatment. Secondary endpoints analyzed were withdrawal from treatment because of treatment failure. A total of 113 patients were enrolled in the study; 56 receiving dexketoprofen (25 mg four times daily) and 57 receiving ketorolac (10 mg four times daily). Group characteristics were comparable at initiation of the treatments. On completion of treatment, the mean PI values were not significantly lower (31.7 versus 39.9 mm for the dexketoprofen and ketorolac groups, respectively; p = 0.12). PRI showed significantly reduced pain (8.8 versus 9.7, p = 0.04). In addition, the dexketoprofen group demonstrated a trend toward fewer withdrawals because of treatment failure (1.8% versus 10.5%, p = 0.11). No differences occurred in reported adverse events for dexketoprofen versus ketorolac. The researchers concluded that dexketoprofen is effective with a good tolerability profile.

Analgesia Is Improved With Combination Oxycodone and Morphine for Cancer Pain

Researchers from the University of Sao Paulo in Brazil presented results from a study comparing the efficacy of controlled-release formulations of morphine or oxycodone alone or controlled-release morphine plus oxycodone. Morphine and oxycodone are opioids that act primarily at μ and k receptors, respectively. The objective of this study was to assess whether the combination of these two opioids acting at different receptors is more effective than each drug given alone. Thirty-six patients were enrolled in the trial. An open-label, randomized titration phase was used initially to achieve pain control for seven days. Then, patients were randomized into a double-blind, crossover phase consisting of two 14-day periods. Throughout the study, patients used oral morphine (10 mg) as needed to keep their pain at less than 4 cm on a visual analog scale (i.e., rescue analgesia). The results demonstrated that rescue analgesia consumption was significantly higher (38%) for patients receiving only morphine compared to those who received a fixed ratio of morphine and oxycodone (ratio 1:1.8). The researchers concluded that the combination of morphine and oxycodone might be a useful alternative to morphine alone with improved analgesia and fewer side effects.

Methadone May Be a Useful Alternative for Cancer Pain

A multinational team from the United States, Serbia, Chile, Colombia, Argentina, Brazil, and Australia presented the results of a study explaining the effectiveness and toxicity of methadone compared to morphine for cancer pain. Ninety-five patients from six centers were randomized into groups to receive either methadone (n = 45, 7.5 mg orally twice daily) or slow-release morphine (n = 50, 15 mg orally twice daily) for four weeks. Breakthrough pain was treated with 5 mg of either drug (depending on group assignment) every four hours as needed. Results from the first week of treatment were presented. Pain was assessed daily using a 0–10 scale. Average baseline pain scores for the methadone group were 7.7 compared to 7.9 for the morphine group. After one week of treatment, no significant differences resulted between the two groups (4.9 versus 4.6 for the methadone and morphine groups, respectively). In addition, no differences existed in reported side effects (e.g., sedation, nausea, confusion, constipation). The researchers concluded that methadone and slow-release morphine have similar effectiveness and side effects, although methadone may be more cost-effective.
Gene Patterns May Identify Likely Responders to Docetaxel

Researchers from Baylor University in Houston, TX, presented the results of a small study of breast tumor tissue from 24 women prior to docetaxel treatment. The researchers used microarray technology to look for patterns of expression of 12,000 genes. Two distinct patterns were found (group 1: n = 13; group 2: n = 11). When these patterns were evaluated in light of responses to docetaxel, researchers found that 10 patients in the first group had good responses and 10 patients in the second group were resistant to treatment. This analysis indicated 83% predictive accuracy for responses. A larger study is in progress to validate these results.

Magnetic Resonance Spectroscopy May Eliminate Lymph Node Surgery

Scientists from the Institute for Magnetic Resonance Research in Sydney, Australia, presented research using a technique for analyzing small clusters of cells obtained with a fine needle. The technique is called magnetic resonance spectroscopy (MRS) and uses computer software to evaluate the likelihood that a malignancy has spread to lymph nodes. Laboratory testing using breast cancer cells demonstrated that MRS can identify benign and malignant tumors and the presence or absence of lymph node involvement with a high degree of accuracy within minutes of obtaining the cell sample. Clinical testing will begin soon in Australia, Sweden, and the United States. The technique has the potential to eliminate unnecessary surgery and complications from lymph node biopsies.

Cancer-Inhibiting Molecule Found in Animal Fat

A minor fatty acid found in meat and dairy products, conjugated linoleic acid (CLA), was shown to inhibit mammary cancer in a rat model. Rat mammary glands contain cells that are multipotent and can develop into fat cells, endothelial cells (i.e., blood vessel lining cells), or fibroblasts. Researchers from Roswell Park Cancer Institute in Buffalo, NY, demonstrated that angiogenesis was reduced by nearly 80% in mice who were fed low levels of CLA for six weeks. Further testing of CLA is ongoing, using a mouse model that overexpresses a protein commonly associated with human breast cancer. Although no toxicities have been reported, considerable additional testing is necessary to evaluate the safety and effectiveness of CLA in breast cancer prevention.

Soy Compound Reduces the Number of Mammary Tumors in Rats

Researchers from the University of Alabama at Birmingham presented a study demonstrating a 50% reduction in the number of mammary tumors in rats who were fed genistein, a soy compound, prior to exposure to a carcinogen compared to those who did not receive genistein. The diet effect was found at specific stages during the animal life cycle: prepuberty alone and prepuberty plus adulthood. Rats in the treatment group were fed 25 mg or 250 mg of genistein per kilogram of diet. This diet produced blood levels similar to those in women who eat a high-soy diet. The carcinogen was administered on day 50, and tumors appeared 40–60 days later. Control rats developed an average of 8.9 tumors and the prepubertal genistein group had an average of 4.3 tumors (51.7% fewer). Those fed the diet during puberty and again as adults had an average of 2.8 tumors (68.6% fewer) after exposure to the carcinogen, indicating an added benefit. Similar results have been reported from other laboratories.

Nodal Biopsy May Improve Survival Rates for Older Women After Breast-Conserving Surgery

A team of researchers from Galveston, TX, matched treatment and outcomes for 31,618 women who had breast-conserving surgery (BCS) for early-stage breast cancer. A total of 9,006 women had BCS without a nodal biopsy; of these, 74% were aged 65 or older and 62% did not receive radiation therapy. The researchers found that nodal biopsy was strongly associated with higher seven-year survival rates and also associated with higher rates of either radiation therapy or chemotherapy. The results suggested that older women may be undertreated for breast cancer, thereby reducing the survival rate in this population.

Zoledronic Acid May Reduce Bone Complications in Patients With Advanced Prostate Cancer

The results of a phase III, randomized double-blind, placebo-controlled trial of zoledronic acid (Zometa<sup>®</sup>, Novartis Pharmaceuticals, East Hanover, NJ) suggested that the drug may reduce bone complications in patients with prostate cancer, such as fractures, spinal cord compression, need for radiation or surgery to bone, or changes in anticancer therapy to treat bone pain. Zoledronic acid currently is indicated as part of the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors. The report was published in the October 2002 issue of the Journal of the National Cancer Institute (Vol. 94, pp. 1458–1468). A total of 643 patients with prostate cancer with progressive disease and at least one bone metastasis were enrolled in the study. The effect of zoledronic acid 4 mg in 100 ml administered over 15 minutes every three weeks for 15 months was compared to administration of a placebo. The results demonstrated that patients receiving zoledronic acid had 25% fewer bone complications compared to the placebo group (33% versus 44%, p = 0.021). The data also demonstrated a delay in the median time to the first skeletal-related event by more than three months for the zoledronic acid group (p = 0.011).

Weekly Vinorelbine and Trastuzumab Is Effective in Treating Metastatic Breast Cancer

A report in the October 28, 2002, issue of The Oncologist (Vol. 7, pp. 410–417) indicated that vinorelbine (Navelbine<sup>®</sup>, Glaxo-SmithKline, Research Triangle Park, NC) in combination with trastuzumab (Herceptin<sup>®</sup>, Genentech, Inc., South San Francisco, CA) improves the overall response rate for patients with metastatic breast cancer. The report, presented by the group leaders at the University of Tennessee College of Medicine, was of a study that involved investigators from seven cancer centers across the United States. A total of 40 women were enrolled in a multicenter, open-label trial. All women had tumors that expressed the Her2-neu oncogene that is the target for the trastuzumab monoclonal antibody therapy. This oncogene product has been associated with poor prognosis for women with breast cancer. Trastuzumab and vinorelbine were given via IV weekly. Thirty-seven patients were evaluated after at least two courses of treatment. Four complete responses and 25 partial responses were found, for an overall response rate of 78%. The median time to progression of the disease was 17 months. Grades three or four neutropenia were observed in 34% of the chemotherapy courses administered. The majority of the nonhematologic adverse events were mild. The authors concluded that the combination of vinorelbine and trastuzumab may improve the overall response rate up to three times more than each agent given alone. A randomized, phase III, multicenter trial is under way.