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RESEARCH HIGHLIGHTS

Sharon Lobert, RN, PhD
Associate Editor

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39th Annual Meeting of the American Society of Clinical Oncology
Chicago, IL
May 30–June 3, 2003

Clinical Research

Chemotherapy May Improve Outcomes for Patients With Resected Non-Small Cell Lung Tumors

The results of the randomized International Adjuvant Lung Cancer Trial were presented by researchers from the Institut Gustave Roussy in Villejuif, France. In this study, 1,867 patients from 148 centers in 33 countries were randomized into two treatment arms: cisplatin-based chemotherapy or no chemotherapy. All patients had complete resection of non-small cell lung carcinomas. A total of 935 patients were allocated to the treatment arm, and 67% received at least 300 mg/m^2 of cisplatin. The drug was combined with etoposide and a vinca alkaloid. The other 932 patients in the control arm did not receive chemotherapy. A significant difference existed between the study arms in the two- and five-year survival rates (70% and 45% in the chemotherapy arm versus 67% and 40% in the control arm; $R^2 = 0.86$, confidence interval = 0.76–0.98, $p < 0.03$). The study arms also differed in the two- and five-year disease-free survival (61% and 39% in the chemotherapy arm versus 55% and 34% in the control arm; $R^2 = 0.83$, confidence interval = 0.74–0.94, $p < 0.003$). Toxicities occurred in the chemotherapy arm, including at least one grade IV toxicity (23%), mainly neutropenia (18%); seven patients (0.8%) died from chemotherapy-related toxicity. The researchers concluded that this study supports the use of adjuvant chemotherapy for patients with resected non-small cell lung carcinomas.

Pemetrexed May Be Effective for Patients With Non-Small Cell Lung Carcinoma

Researchers from Indiana University presented the results of a multicenter, phase III trial of pemetrexed versus docetaxel for patients with recurrent non-small cell lung cancer. Pemetrexed is an inhibitor of folic acid synthesis. Folic acid is essential for cell growth, and pemetrexed interferes with the activity of three enzymes necessary for cell division. A total of 571 patients who had been treated previously with chemotherapy were randomized into one of two treatment groups: pemetrexed 500 mg/m^2 IV supplemented with vitamin B_{12} injections, folic acid, and dexamethasone, or docetaxel 75 mg/m^2 IV with dexamethasone on day one of 21-day cycles. Ten months after the final patient entered the study, 52% (299 patients) had died. Toxicities included neutropenia (40%), neutropenia fever (7%), anemia (6%), fatigue (5%), anorexia (2%), nausea (2%), thrombocytopenia (2%), diarrhea (1%), neuropathy (1%), and hypersensitivity (< 1%). For all patients, 43% had stable disease. Partial or complete remission occurred in 9% of patients taking pemetrexed and 9% of patients taking docetaxel. Patients taking pemetrexed were less likely to experience severe chemotherapy-related side effects such as fever and infections, be hospitalized because of side effects, or experience hair loss or peripheral neuropathy. The researchers concluded that because of the reduction in side effects, pemetrexed might replace docetaxel for recurrent non-small cell lung cancer.

Epidemiologic Research

Survey Indicates Need for Cancer Prevention Education

A survey conducted by the American Society of Clinical Oncology and the Cancer Research and Prevention Foundation indicated that the public might be confused regarding what steps are necessary for cancer prevention. The purpose of the Cancer Prevention Survey was to assess attitudes and perceptions about cancer prevention. Telephone interviews of a random sample of adults aged 18 and older (n = 1,000) were conducted in April and May 2003. Primary care physicians (n = 150) also were surveyed regarding cancer prevention attitudes and practices. The results showed that 88% of the respondents believed that they could take actions to reduce their risk for developing cancer; however, their understanding of specific actions to take varied. For example, only 38% thought that eating fresh fruits and vegetables could lower their risk and only 33% believed that maintaining a healthy weight would be effective. Scientific evidence does show that diets that include fresh vegetables and fruits and reduced animal fat or calories are associated with reduced risk of developing some cancers. Maintaining a healthy weight appears to reduce the risk of colon, pancreatic, breast, and other cancers. Slightly more than half of the respondents agreed that cancer risk could be reduced by exercise. Because of the importance of weight control, current recommendations for a healthy lifestyle and cancer risk reduction include at least 30 minutes of exercise per day five or more days per week. Although scientific evidence does not support the use of herbal supplements to reduce cancer risk, nearly 30% of the respondents strongly agreed that taking vitamins or herbal supplements would be effective. The Cancer Prevention Survey also found some disparity between the information that physicians believe they are providing concerning preventive cancer risk behaviors and the information that patients report receiving. Physicians reported counseling 75% of their patients regarding cancer risk; however, only 45% of the respondents reported that a healthcare professional had spoken to them about cancer prevention. These survey results indicate that much work must be done to dispel myths regarding cancer risks and prevention behaviors and to consistently provide accurate information to help patients choose healthier lifestyles.

94th Annual Meeting of the American Association for Cancer Research
Washington, DC
July 11–14, 2003

Basic Research

New Antiangiogenesis Therapy Shrinks Liver Tumors in Mice

The Tie2 receptor protein in endothelial cells regulates the cellular response to vascular endothelial growth factor (VEGF) that is secreted by malignant cells to grow and maintain blood vessels. Angiopoietin 2 binds to the Tie2 receptor, resulting in the signal for blood vessels to grow. Blocking the Tie2 receptor could limit tumor growth. Researchers from Duke University developed mouse colon cancer cells that secreted

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Digital Object Identifier: 10.1188/04.ONF.25-26

a soluble version of VEGF and Tie2 receptors. Colon cancer cells with and without these soluble receptors were delivered via intrasplenic injection into BALB/c mice to induce liver metastases. Tumor growth was reduced significantly in mice that expressed the soluble Tie2 or VEGF receptors (76% reduction compared to control mice at 28 days [$p < 0.05$]). The mean survival time for mice expressing the soluble receptors also was increased (51.3 and 46.4 days for Tie2- and VEGF-expressing mice compared to 28.6 days for control mice [$p < 0.01$]). These data support the VEGF pathway as a target for antiangiogenesis therapy. The data also suggest that Tie2 may be a useful target for these molecular therapies.

Interaction of Two Genes May Increase Risk of Lung Cancer

Researchers from the University of Pittsburgh presented preliminary results of a study examining the interaction of two genes that may contribute to lung cancer risk. Cell samples from 357 participants (173 with lung cancer and 184 healthy individuals) were examined for mutations in a DNA repair gene, *XPD,* and the gene for cyclin D1, *CCND1.* DNA repair genes such as *XPD* ensure that genetic information is copied correctly when cells divide. *CCND1* is a cell-cycle regulator, and its activity is important for DNA repair before cell division. The study showed that mutations in both of these genes occurred more often in patients who had lung cancer compared to the control group. Furthermore, individuals with mutations in both genes plus a smoking history had an odds ratio of 17.0 for lung cancer risk compared to nonsmokers who had an odds ratio of 6.3, indicating a significantly higher risk of lung cancer for smokers. The researchers suggested that the findings from this study might help to identify biomarkers that indicate high risk of lung cancer and thereby have an impact on morbidity and mortality.

Additional Research Highlights

Addition of High-Dose Chemotherapy Does Not Improve Outcomes for Patients With Breast Cancer

The results of a multicenter randomized trial of conventional adjuvant chemotherapy with or without high-dose chemotherapy and autologous stem-cell transplantation were presented in the July 3, 2003, issue of the *New England Journal of Medicine* (Vol. 349, pp. 17–26). In this study, 540 women with primary breast cancer and at least 10 involved ipsilateral axillary lymph nodes were divided into one of two treatment groups: six cycles of adjuvant chemotherapy with cyclophosphamide, doxorubicin, and fluorouracil, or the same adjuvant therapy followed by high-dose chemotherapy with cyclophosphamide, thiotepa, and autologous hematopoietic stem-cell transplantation. The researchers found no significant differences in disease-free survival, overall survival, or time to recurrence between the two groups. They concluded that the addition of high-dose chemotherapy and autologous hematopoietic stem-cell transplantation to six cycles of adjuvant chemotherapy does not improve outcomes. Conventional-dose adjuvant chemotherapy should remain the standard of care for patients with primary breast cancer and involvement of at least 10 lymph nodes.

COX-2 Inhibitor May Enhance Response to Preoperative Paclitaxel and Carboplatin for Non-Small Cell Lung Cancer

Researchers at Cornell University in New York City reported in the July 14, 2003, issue of the *Journal of Clinical Oncology* (Vol. 21, pp. 2645–2650) the results of a phase II clinical trial of two preoperative cycles of paclitaxel, carboplatin, and celecoxib (400 mg twice daily) for the treatment of non-small cell lung cancer (NSCLC). Chemotherapy was followed by surgical resection. Celecoxib is a selective cyclo-oxygenase-2 (COX-2) inhibitor that reduces the production of prostaglandin E_2 (PGE_2). PGE_2 levels have increased in primary tumors after treatment with paclitaxel and carboplatin. Preclinical studies suggested that celecoxib might enhance the antitumour effects of chemotherapy. The trial enrolled 29 patients with stages IB–IIA NSCLC. The end points examined were toxicity, response rates, and intratumoral levels of PGE_2. The overall clinical response rate was 65% (48% complete and 17% partial). Eighteen patients (62%) had grade III or IV neutropenia. By pathologic criteria, no complete responses occurred; however, seven patients (24%) showed minimal residual microscopic disease. The addition of celecoxib to the chemotherapy regimen lowered the intratumoral PGE_2 levels. These data were compared with previously reported response rates. The researchers suggested that celecoxib might enhance the response to preoperative paclitaxel and carboplatin in patients with NSCLC. Treatment with 400 mg celecoxib twice daily normalized the intratumoral PGE_2 levels. Additional studies are planned.

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