NOVEMBER IS LUNG CANCER AWARENESS MONTH: *How Far Have We Come?*

As Lung Cancer Awareness Month comes to an end, I would like to reflect on how far we have come in managing this disease. For about 30 years, progress in treating lung cancer was quite slow, until very recently. Only 15 percent of patients with lung cancer survive for five years, and the number of deaths annually exceeds the combined total for breast, prostate, and colon cancer. Even when surgical resection of lung tumors is possible, which can improve five-year survival rates up to 60 percent, death usually results from recurrence at sites outside the lungs. Over the past year, we have made enormous strides in identifying and understanding molecular targets for treating non-small cell lung cancer (NSCLC). Perhaps the most successful of these has been the positive clinical response to drugs targeting specific mutations in the epidermal growth factor receptor (EGFR) among patients with advanced NSCLC who have failed previous chemotherapy regimens.

Recent studies have made substantial gains in identifying subgroups of patients with advanced NSCLC who are the most likely to respond to EGFR tyrosine kinase inhibitors such as gefitinib and erlotinib. In Taron and colleagues' recent seminal study of gefitinib, published in August in *Clinical Cancer Research,* 94 percent of patients with EGFR mutations responded strongly to gefitinib compared with only 13 percent of those without such mutations. Certain subgroups of patients—those who had never smoked, had already undergone intensive treatment, were Asian, or were younger—had the highest response rates to gefitinib. Median survival increased from the typical seven or eight months to about two years in patients with mutation-positive tumors. Similarly, Shepherd and colleagues reported this year in *New England Journal of Medicine* (2005;353:123-32) that erlotinib extended survival while relieving symptoms such as cough, shortness of breath, and pain in patients who had failed first- and second-line treatment for NSCLC. Subsequent studies of the mechanisms of action of erlotinib suggested that this drug also targets additional unknown signaling pathways that drive tumor-cell proliferation.

According to Sequist and colleagues *(Clinical Cancer Research* 2005;11:5668-70), these and other promising studies have led more and more clinicians to recommend starting treatment with EGFR tyrosine kinase inhibitors earlier in responsive patients with NSCLC, as first-line treatment for advanced disease and adjuvant therapy for early stage, surgically treated disease. Several large clinical studies are currently underway to test the effectiveness of first-line therapy with gefitinib, with or without chemotherapy or surgery, in selected subgroups of patients who have EGFR mutations. Recent investigations provide further evidence that cancer therapies may be more effective when they are personalized to the molecular characteristics of each patient's malignant disease.

Another area of progress this year with marked potential to improve survival in early-stage NSCLC is the clear benefit of adding chemotherapy after surgical resection. Until recently, the survival benefit of adjuvant chemotherapy has been uncertain. Results of adjuvant chemotherapy in clinical trials have been inconsistent, ranging from worse survival rates to very small gains in five-year survival, attributed mainly to poor and inconsistent study design or the addition of radiotherapy to the treatment regimen. In June of this year, however, Winton and colleagues reported astonishing five-year survival benefits in the *New England Journal of Medicine* (2005;352:2589-97). Their randomized clinical trial with 482 patients demonstrated that, compared with surgery alone, adjuvant vinorelbine combined with cisplatin significantly prolongs both disease-free and overall survival among patients with completely resected, early-stage, NSCLC. An astounding 69 percent of patients who received chemotherapy were still alive five years later, compared with 54 percent who underwent surgical resection only, while risk of death decreased 31 percent. This 15 percent survival advantage clearly exceeds the small benefits of four or five percent reported in earlier large clinical trials. Benefits of similar adjuvant chemotherapy regimens were reported at the annual meeting of the American Society of Clinical Oncology (ASCO) in May 2005, particularly from the large Adjuvant Navelbine International Trialist Association (ANITA) studies. Based on the evidence, I believe that adjuvant platinum-based chemotherapy should be recommended after complete resection of non-small-cell lung cancer in patients with a good performance status. This represents a giant leap forward in the outlook for a disease that has seen little progress over the past few decades.

"The controversy surrounding adjuvant chemotherapy for resectable non-small-cell lung cancer is over," concurred Katherine Pisters, M.D., professor, Department of Thoracic/Head and Neck Medical Oncology, in her accompanying editorial in the *New England Journal of Medicine* (2005;352:2640-2) and DoCM Grand Rounds presentation Sept. 20th. Looking forward to future advances, Dr. Pisters added, "Additional research will enable us to select those patients most likely to benefit from adjuvant therapy, to customize the therapy on the basis of the biology of the tumor, to lessen toxicity and increase compliance, to identify more effective regimens, and to further improve survival."

Other areas of progress in lung cancer research will also be presented December 5th on Science Day for Lung Cancer Research.

COMING UP

- On Monday, Dec. 5th, the Thoracic/Head & Neck Medical Oncology department will host "Science Day for Lung Cancer Research 2005" at the Hickey Auditorium, R11.1400, from 7 a.m. to 4:45 p.m. Waun Ki Hong, M.D., division head, will give opening remarks along with John Mendelsohn, M.D., president. Speakers will lead discussions about the advances, problems, and prospects in experimental, translational, and clinical aspects of lung cancer research, specifically four programs funded by the Department of Defense: BESCT, TARGET, VITAL, and IMPACT.

  To register, log onto http://www2.mdanderson.org/depts/cancermed/scienceday/.

- Dr. Hong will give his annual state-of-the-division address on **Tuesday, Dec. 20th** at 8 a.m., at the Hickey Auditorium, R11.1400. In addition, R11.1100, rooms 1–4, will be used for overflow seating. Dr. Hong will highlight DoCM achievements in 2005 in organizational structure, patient care, financial performance, education and training, and research, as well as present division goals for 2006.