

Research Updates January 2004

Trastuzumab (Herceptin®) Adds Little to Effects of Standard Chemotherapy for Advanced NSCLC

Researchers from Germany have announced results from a phase II clinical trial that studied the effects of trastuzumab (Herceptin®) in combination with standard chemotherapy for the treatment of advanced NSCLC. The study of 100 people found the addition of trastuzumab led to no significant improvements over chemotherapy alone.¹ While the results were disappointing, researchers stated there may still be a role for trastuzumab (a monoclonal antibody) among people whose lung cancer expresses very high levels of HER-2.

Low Tar Cigarettes Do Not Decrease Risk of Lung Cancer

A large study involving over 940,000 participants found the risk of lung cancer is the same among people who smoke medium tar, low tar, and very low tar cigarettes.² These findings are contrary to tobacco companies' advertising of "light" and "ultra light" cigarettes. Dr. Michael Thun of the American Cancer Society said, "There was not a shred of evidence of reduced risk [with low tar cigarettes]." However, investigators did note a higher risk for lung cancer among people who smoked unfiltered cigarettes compared to those who smoked filtered cigarettes. All findings were the same for men and women.

Surgeons' Lung Cancer Experience Linked to Outcomes for People with Limited, SCLC

A study presented at the Society of Thoracic Surgeon's annual meeting in January 2004 found surgeons specializing in lung cancer were more likely to achieve a successful resection of limited small cell lung cancer than surgeons who did not specialize in lung cancer.³ While postoperative, in-hospital deaths were the same in both groups (3%), people operated on by lung cancer specialists survived significantly longer than those whose surgeon was not a lung cancer specialist (18 versus 8 months). Although the study was relatively small (70 patients), the findings are important for people considering surgical treatment for SCLC.

New England Journal of Medicine Publishes Study Showing Survival Advantage with Postoperative Chemotherapy for People with Resected NSCLC

A large study of 1,867 people who had undergone a complete resection for NSCLC randomly assigned participants to either observation or postoperative (adjuvant) platinum-based chemotherapy. The published results, which were previously reported at cancer meetings in 2003, showed people assigned to chemotherapy had a significantly higher 5-year survival rate (44.5%) than those assigned to observation (40.4%).⁴ The authors concluded, "... our results strongly support the use of three or four cycles of cisplatin-based chemotherapy after complete surgical resection in patients with non-small-cell lung cancer."

Research Updates January 2004

Treatment Outcomes Similar for Chemotherapy Plus Surgery Versus Concurrent Chemoradiotherapy for Stage IIIA NSCLC

A recent study at the University of Texas M. D. Anderson Cancer Center compared the outcome of preoperative (induction) chemotherapy followed by surgery (C/S) to concurrent chemoradiotherapy (CRT) among 107 people with stage IIIA NSCLC. Researchers found no significant differences between the two treatment groups in terms of local control, survival time, 5-year overall survival, distant metastasis-free survival, and disease-free survival.⁵ The authors suggested that recent advances in radiation-based treatment have resulted in similar outcomes with CRT compared with modern induction chemotherapy plus surgery.

Study Finds Mediastinoscopy Superior to PET for NSCLC Staging

Investigators at Duke University Medical Center compared the accuracy of positron emission tomography (PET) to mediastinoscopy for the mediastinal staging of 202 people with NSCLC. Participants first underwent a PET scan followed by a mediastinoscopy. Results of the two procedures were then compared. Of the 65 people with positive results by PET, only 29 (44.6%) had positive results by mediastinoscopy. Of the 137 people with negative PET results, 16 (11.7%) had positive results by mediastinoscopy.⁶ Based on their findings, the authors concluded, "PET neither confirms nor excludes involvement of the mediastinum in patients with NSCLC. Cervical mediastinoscopy with lymph node biopsy remains the standard for mediastinal staging."

Preliminary Results of Phase II Study of Docetaxel (Taxotere®) plus Enoxaparin (Lovenox®) Suggest Possible Role in Metastatic NSCLC

Activation of coagulation appears to play a role in tumor progression. Enoxaparin (Lovenox®) is an anticoagulant that was tested in combination with docetaxel in this trial among 15 people with stage IV NSCLC. Eight patients on the drug combination had an objective response (53%) and four had stable disease. The median time to disease progression was 5 months and the median survival time was 11 months.⁷ Based on these preliminary results, the authors concluded the combination of docetaxel plus enoxaparin is safe and well tolerated in people with advanced NSCLC. They also stated the data suggest that enoxaparin may prolong the time to disease progression. Additional research is needed to determine if enoxaparin may improve treatment outcomes among people with advanced NSCLC.

New Practice Guideline Recommends Etoposide-Cisplatin as the Preferred Chemotherapy Regimen for People with Limited-Stage SCLC Undergoing Concurrent Radiotherapy

Cancer Care Ontario recently conducted a review of 50 randomized trials conducted from 1985 through 2002 addressing the first-line treatment of limited small-cell lung cancer. Based on the evidence from these studies, the new

Research Updates January 2004

practice guideline recommends etoposide-cisplatin is the preferred chemotherapy regimen for people with limited-stage SCLC when concurrent thoracic radiotherapy is used.⁸ The guideline further states that it is reasonable to offer the alternation of etoposide-cisplatin with cyclophosphamide-doxorubicin-vincristine, provided the administration of radiotherapy concurrent with an anthracycline (such as doxorubicin) is avoided. Guideline authors also note the use of maintenance chemotherapy is not indicated for people with limited SCLC. While clinical trials of other chemotherapy regimens are important in the search for more effective treatment options, this guideline gives both doctors and patients a thorough review of the evidence to date.

Second-Line Docetaxel (Taxotere®) Improves Survival and May Improve Quality of Life in NSCLC

A phase III trial comparing second-line docetaxel (Taxotere®) versus best supportive care among 204 people with NSCLC found docetaxel improved survival and showed a trend toward less deterioration in quality of life (QOL).⁹ There was a significant difference in favor of docetaxel in terms of patient-reported pain, and trends in favor of docetaxel regarding appetite and fatigue.

Advanced Age Does Not Preclude Surgery for Lung Cancer

A study from Johns Hopkins that examined the outcomes for 68 people in their eighties who underwent surgery for NSCLC found that 1-, 3-, and 5-year survival rates were comparable to those of younger patients when matched for stage, performance status, and respiratory (breathing) function.¹⁰ These data support earlier studies that have concluded chronological age alone is not a contraindication to surgical treatment of lung cancer.

- 1 Gatzemeier U, Groth G, Butts C, et al. Randomized phase II trial of gemcitabine–cisplatin with or without trastuzumab in HER2-positive non-small-cell lung cancer *Ann Oncol*. 2004;15:19-27.
- 2 Harris JE, Thun MJ, Mondul AM, Calle EE. Cigarette tar yields in relation to mortality from lung cancer in the cancer prevention study II prospective cohort, 1982-8. *BMJ*. 2004;328:72.
- 3 Hoffstetter WL, et al. Surgeons Specializing in Lung Cancer Perform Higher Quality Resections. 40th Annual Meeting of the Society of Thoracic Surgeons. Abstract 38. January 2004. San Antonio, Texas.
- 4 Arriagada R, Bergman B, Dunant A, Le Chevalier T, Pignon JP, Vansteenkiste J. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. *N Engl J Med*. 2004;350(4):351-60.
- 5 Taylor NA, Liao ZX, Cox JD, et al. Equivalent outcome of patients with clinical Stage IIIA non-small-cell lung cancer treated with concurrent chemoradiation compared with induction chemotherapy followed by surgical resection. *Int J Radiat Oncol Biol Phys*. 2004;58(1):204-12.
- 6 Gonzalez-Stawinski GV, Lemaire A, Merchant F, O'Halloran E, Coleman RE, Harpole DH, D'Amico TA. A comparative analysis of positron emission tomography and mediastinoscopy in staging non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2003;126(6):1900-5.
- 7 Robert F, Busby E, Marques MB, Reynolds RE, Carey DE. Phase II study of docetaxel plus enoxaparin in chemotherapy-naïve patients with metastatic non-small cell lung cancer: preliminary results. *Lung Cancer*. 2003;42(2):237-45.

Research Updates January 2004

- 8 Laurie SA, Logan D, Markman BR, Mackay JA, Evans WK. Practice guideline for the role of combination chemotherapy in the initial management of limited-stage small-cell lung cancer. *Lung Cancer*. 2004;43(2):223-40.
- 9 Dancey J, Shepherd FA, Gralla RJ, Kim YS. Quality of life assessment of second-line docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy: results of a prospective, randomized phase III trial. *Lung Cancer*. 2004;43(2):183-94.
- 10 Brock MV, Kim MP, Hooker CM, et al. Pulmonary resection in octogenarians with stage I nonsmall cell lung cancer: a 22-year experience. *Ann Thorac Surg*. 2004;77(1):271-7.