Commentary (Greco)—Limited Small-Cell Lung Cancer: A Potentially Curable Disease

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Patients with limited-stage small-cell carcinoma of the lung are treated with combined-modality therapy with the intent to cure. Standard therapy consists of platinum-based combination chemotherapy, thoracic irradiation, and

Drs. Sherman and colleagues provide a well-written, fairly extensive review of limited-stage small-cell lung cancer. This commentary will address a few other issues involved in the diagnosis and treatment of this disease.

Traditional Definition of Limited Disease
The authors did not discuss patient subsets with “limited-stage disease.” There are now more than enough data available to begin staging or classifying patients with small-cell lung cancer using the revised international TNM staging system.[1] We seem, however, to be historically shackled to the concept of limited- and extensive-stage disease, which includes several important patient subsets. Particularly useful for patients with limited-stage disease, TNM staging provides a reproducible classification system for groups of patients who are otherwise often inconsistently identified and defined.

Drs. Sherman et al discuss some of the disagreements regarding the definition of limited-stage disease. Although most limited-stage patients present with clinical stage IIIA or IIIB disease, a minority of patients present with stage IA, IB, IIA, or IIB disease. In general, these patients with earlier-stage disease fare better with the same therapies, but the data for this group are extremely difficult to cull from past publications.

An important issue for earlier-stage patients (ie, T1N0, T2N0, T1-2N1, T3N0-1) is a mistaken diagnosis, particularly confusion with other neuroendocrine tumors of the lung (carcinoids, atypical carcinoid, mixed small-cell/large-cell carcinomas) after fine-needle aspiration and subsequent implications for surgical resection. Well-differentiated carcinoid tumors do not require chemotherapy and are best treated by removal. Stage I (IA or IB) patients with histologically documented small-cell lung cancer also require initial surgical resection.

Based on older data,[2] most oncologists now recommend surgical resection, which allows for good local therapy and more precise histologic documentation. If a diagnosis of small-cell carcinoma is confirmed, postoperative adjuvant chemotherapy is administered. Resection is therefore important for a relatively small group of patients, who can be identified and accurately documented with the help of TNM staging.

Studies of surgery following chemotherapy and radiation therapy for the more common limited-stage patient with stage III disease have shown no apparent survival advantage.[3] However, by today’s standards, these studies were performed with suboptimal chemotherapy and radiation therapy.

Poor Performance Status in Limited-Stage Patients
Unfortunately, a substantial number of patients with earlier stages of small-cell lung cancer present with poor performance status. Many of these patients are elderly or suffer from comorbid illnesses, particularly chronic-obstructive pulmonary disease and cardiac disease. It is unrealistic to expect these patients to be treated with the intensive combined-modality programs as outlined by Dr. Sherman and coauthors.

For these patients, we need to consider and study other approaches, such as newer drugs—particularly paclitaxel (Taxol), docetaxel (Taxotere), or vinorelbine (Navelbine), given on a weekly schedule, perhaps with low-dose, weekly carboplatin (Paraplatin). Concomitant radiation might also be considered in some of these patients. Other approaches might include the sequential use of less-toxic chemotherapy followed by definitive radiation therapy. Of course, some patients with poor performance status are not potentially curable and are candidates for palliative chemotherapy only.

Targeted Therapies
The rather rapid elucidation and understanding of the various aspects of neoplastic development and growth, including patients with all varieties of lung cancer, have created an environment conducive to the development of relatively targeted approaches to treatment. This era is already underway, as evidenced by the use of the monoclonal antibodies rituximab (Rituxan) and trastuzumab (Herceptin). Additionally, several currently available products target important aspects of neoplastic growth, including inhibition of angiogenesis and various growth factors,[4] as well as tumor vaccines made from specific tumor antigens. Several of these compounds (eg, anti-vascular endothelial cell growth factor [VEGF] antibody, anti-epidermal growth factor receptor [EGFR] antibody, and several vaccines) are now actively being tested in patients with non-small-cell lung cancer. These and other compounds will soon provide a more specific targeted approach to the treatment of patients with small-cell lung cancer. Patients with earlier (limited-stage) disease who have responded well to standard cytotoxic approaches will be the ideal candidates in whom to test some of these targeted therapies.

A further basic understanding might enable various growth-inhibiting proteins and even fragments of genetic material (such as active tumor suppressors) to be delivered in a specific fashion that will abrogate further growth of small-cell lung cancer. Indeed, this concept is no longer purely theoretical, since more specific targeted oncologic therapies are now available, and it is expected that many more will be tested in the near future.

References:


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