Commentary (Hansen)—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

The article by Sherman et al is a broad review of the recent developments in the treatment of patients with small-cell lung cancer who present with limited disease. Initially, the authors emphasize that the increasing use of more intensive and refined staging procedures, such as computed tomography (CT) scan and, more recently, positron-emission tomography (PET) scan, have resulted in stage migration. This phenomenon has led to improved outcomes of both limited and extensive disease, but has not necessarily improved overall survival.

Further refinement of staging is expected with the use of various monoclonal antibodies to identify tumor cells in bone marrow or to detect occult micrometastasis in lymph nodes by a reverse transcriptase polymerase chain reaction. The prognostic value of the detection of small numbers of tumor cells in the bone marrow has recently been demonstrated by Pasini et al.[1] In addition, we can expect an increased use of magnetic resonance imaging (MRI) in the detection of brain metastases.

Advances in Treatment

With respect to treatment, emphasis is placed on the importance of the combined use of combination chemotherapy with chest irradiation and prophylactic cranial irradiation. In particular, the issue of timing of the treatment modality with chemotherapy is also discussed. I can only agree with the authors that with respect to optimal timing of thoracic radiation, no firm conclusions can be drawn at present.

Highly encouraging are the results of using twice-daily chest irradiation combined with cisplatin (Platinol) and etoposide, resulting in a 5-year survival of 26% compared to 16% with chest irradiation given once daily. Confirmation of these results is needed, because neither Bonner et al[2] in the North Central Cancer Treatment Group (NCCTG) study nor Mennecier et al[3] from France have been able to produce similar results. These differences in results may be attributed to variations in the study design. The Bonner study used a break in the delivery of thoracic irradiation at approximately the midperiod of the radiotherapy schedule, whereas Turrisi et al[4] did not use such a break. The NCCTG study also used chest irradiation at an earlier stage (chemotherapy cycle 1 or 2) than the Turrisi study (cycle 4 or 5). Finally, the thoracic irradiation field was different, with the NCCTG study encompassing only the postchemotherapy tumor volume in the field. The latter resulted in less toxicity but was perhaps associated with a higher failure rate. In the French study, differences in the results might exclusively be a question of patient selection, with the French study including more patients with poor prognostic factors.

Regarding local treatment, it should be remembered that a small proportion (5%) of patients with small-cell lung cancer present with stage I or II disease. For this group, surgery followed by chemotherapy is indicated, which yields a 5-year survival rate of 25% to 70%. This is similar to the result for non-small-cell lung cancer patients presenting with the same stage.[5]

The combination of etoposide and cisplatin is the most commonly used chemotherapy regimen and, in most countries, the one considered to be the standard treatment for limited disease when administered together with radiotherapy. The authors’ statement that a combination of carboplatin (Paraplatin) and etoposide might be equally effective was recently challenged at the 9th World Conference on Lung Cancer in Tokyo, September 2000.[6] A total of 34 patients received etoposide, 120 mg/m² intravenously (IV) on days 1, 3, and 5, and cisplatin, 100 mg/m² on day 1. The other 34 patients received the same dose of etoposide and carboplatin, 400 mg/m² on day 1. The median survival was 15 months vs 10 months ($P < .05$).
Promise of Newer Agents
As mentioned by the authors in this article, real progress in the treatment of small-cell lung cancer has been modest during the last 20 years, and the development of new cytostatic agents with activity against resistant cells is needed. In the 1990s, a series of new agents were tested, such as the taxanes (paclitaxel [Taxol] and docetaxel [Taxotere]) and topoisomerase I inhibitors (topotecan [Hycamtin] and irinotecan [Camptosar]). Among these, irinotecan appears especially promising.

In a two-armed Japanese study with 77 patients in each arm, the median survival and 1-year survival rate were 411 days and 56% in the irinotecan/cisplatin arm vs 282 days and 34% in the etoposide/cisplatin arm ($P = .00025$ for survival, one-sided log-rank test).[7] Further studies with irinotecan and the other new agents are awaited with interest.

In addition to the positive development of new classical cytostatic agents, it is encouraging to note that ongoing testing of metalloproteinase inhibitors and tumor-tailored gene therapy is taking place. These are all attempts to increase the present cure rate for the most devastating of all pulmonary carcinomas: small-cell lung cancer.

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