Retreatment of Patients Surviving Cancer-Free 2 or More Years After Initial Treatment of Small Cell Lung Cancer

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Study objective: To assess the outcome after retreatment of patients with small cell lung cancer (SCLC) who redevelop small cell cancer (SCC) 2 or more years after initial therapy.

Setting: Single government institution: the National Cancer Institute.

Patients: Twenty patients who redeveloped SCC among 65 patients who survived 2 or more years after starting treatment for their initial cancer.

Measurements: The response rate of patients after retreatment, the survival duration from the time of redevelopment of SCC, and the toxicities of retreatment.

Results: Twenty patients redeveloped SCC: 18 with a relapse and 2 with a second primary cancer. Sixteen received treatment after they redeveloped SCLC while four did not. Eleven patients were retreated with chemotherapy alone, two patients received chemotherapy plus chest radiotherapy, one patient received radiotherapy alone, one patient underwent lobectomy, and one patient was treated with a monoclonal antibody followed by chemotherapy. Nine of 16 patients (56%) treated after they redeveloped SCLC had an objective response (3 complete and 6 partial). The median survival of all 20 patients after they redeveloped SCC was 3.9 months (range, 0 to 46 months). The median survival of the patients who were retreated was 6.5 months (range, 1 to 46 months).

Conclusions: Patients who suffer relapses with SCLC 2 or more years from diagnosis are candidates for retreatment.

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Small cell lung cancer (SCLC) represents approximately 20% of all lung cancers.1 Fifteen to 25% of patients with limited-stage SCLC and up to 3% of patients with extensive-stage disease will be alive and cancer-free 2 years after treatment with combination chemotherapy.1,3 Approximately one third of these patients will suffer a relapse with SCLC after 2 years.1,4,6

There are relatively little data on the results of subsequent treatment of these patients.

A prior report in 1983 of 6 patients from this institution described the initial experience with retreatment of patients surviving SCLC for 2 or more years. Four of the 6 patients retreated with combination chemotherapy had a partial or complete response and achieved a median survival of 10 months from the start of retreatment.7 This success in retreatment is in contrast to the experience with patients with SCLC whose cancer relapses shortly after induction therapy in whom retreatment has been only minimally successful.8,9

Recent studies have shown a higher proportion of patients treated for limited-stage SCLC survive for 2 or more years. Patients with limited-stage SCLC treated with etoposide/cisplatin (EP) plus chest radiotherapy have achieved 36 to 56% 2-year survival after...
initial treatment. Therefore, more patients are at risk for late relapses of SCLC. In addition, most patients with limited-stage disease have been initially treated with chemotherapy plus chest radiotherapy which causes more hematologic toxicity than chemotherapy alone. The increased use of combined-modality therapy will likely reduce a patient’s ability to tolerate retreatment with chemotherapy.

We have identified patients who have redeveloped small cell cancer (SCC) after surviving cancer free for 2 or more years from their initial treatment. The outcome of all patients who redeveloped SCC has been followed, including both those who received retreatment and those who did not. The patient characteristics, regimens administered, hematologic toxic reactions encountered, response to therapy, and survival duration before and after redevelopment of SCC were determined for each patient.

MATERIALS AND METHODS

Patient Population

Patients with histologically confirmed, previously untreated SCLC were enrolled on National Cancer Institute (NCI) intramural therapeutic trials between 1973 and 1993. These trials were approved by the Institutional Review Boards at the NCI, National Naval Medical Center, and the Washington, DC Veterans Administration Medical Center; informed consent was obtained from each patient. All had primary SCLC with assessable tumor lesions; none were treated in an adjuvant setting after surgical resection. Patients underwent assessment of disease sites and were classified as having either limited- or extensive-stage disease as previously defined. Initial sites of SCLC were identified as previously described. Patients received treatment with combination chemotherapy with or without radiotherapy with a variety of regimens that have been previously reported. The response to treatment and current status of all patients were determined.

Retreatment of Patients With Redevelopment of SCC

Patients surviving for 2 years or longer without evidence of cancer were identified. The patients’ characteristics at the time of redevelopment of SCC and duration from initial chemotherapy treatment were obtained from the patients’ records. The time to redevelopment was measured from the start of chemotherapy to the date of histologic documentation of redevelopment of SCC. The doses of chemotherapy agents used at the time of redevelopment of SCC, doses of chest radiotherapy, and hematologic toxicity of retreatment were obtained through review of patient records. Toxicity during retreatment was measured using the NCI common toxicity criteria. The response to retreatment was assessed as previously described.

The survival after redevelopment of SCC was measured from the date of redevelopment of cancer in all patients. Survival curves were constructed using the method of Kaplan and Meier. The p value for the comparison of survival duration between patients retreated with etoposide-containing regimens and those who did not receive etoposide is derived from the likelihood ratio test of the Cox proportional hazards model. The p value for the comparison of response rates in retreated patients is derived from Fisher’s exact test. The measured times to redevelopment of SCC were logarithmically transformed before analysis in order to make their distribution more uniform.

RESULTS

Patient Characteristics at Initial Diagnosis

Five hundred ninety-four patients with SCLC were consecutively enrolled on therapeutic trials between 1973 and 1993. The median potential follow-up period of the 594 patients was 14.8 years and the minimum follow-up was 2 years.

Sixty-five patients (11%) were alive and free of cancer 2 years after the initiation of therapy. The other 529 patients died or had suffered relapses with SCLC before 2 years. Twenty of the 65 patients (31%) who survived cancer free for 2 years from initial diagnosis redeveloped SCC 2.0 to 12.2 years (median, 3.4 years) after initiation of therapy for SCLC (Table 1). Among these 20 patients, there were 11 men and 9 women. The median age of these patients was 59 years (range, 35 to 69 years). Fifteen patients had limited-stage SCLC and five had extensive-stage disease after initial staging evaluation. Chemotherapy administered to the patients after initial diagnosis of SCLC was cyclophosphamide, methotrexate, lomustine (CCNU)/vincreistine, doxorubicin, procarbazine (CMC/VAP) in seven patients, cyclophosphamide, doxorubicin, procarbazine, vincristine (CAPO) in two, cyclophosphamide, doxorubicin, vincristine (CAV) in five, and EP in six patients (Table 1). Fourteen of the 15 patients with limited-stage disease were treated with chest radiotherapy as part of induction therapy. Initial response assessment showed a complete response in all 20 patients.

Patient Characteristics at the Time of Redevelopment of SCC

The median age of the 20 patients at the time of redevelopment of SCC was 63 years (range, 39 to 81 years). Performance status was 0 or 1 in 10 patients, 2 in 5 patients, and 3 or 4 in 4 patients (Table 1). Patient 3 was discovered to have SCC at postmortem examination and was scored as performance status 5. Only 1 of the 20 patients did not have histologic documentation of redevelopment of SCC. This patient redeveloped a mediastinal mass in the same site of previous cancer and required urgent therapy because of superior vena cava syndrome. The sites of redevelopment of SCC in each patient have been published previously. Nine patients redeveloped SCC in the chest only; seven patients redeveloped SCC outside the chest, and four patients developed SCC both within and outside the chest. Thirteen patients had the equivalent of extensive-stage disease and seven patients had the equivalent of limited disease at the time of redevelopment of SCC.

Two patients were judged to have second primary SCCs. Patient 3 developed SCC of the esophagus 5.9 years after the start of treatment, with no other
Table 1—Characteristics of 20 Patients With SCLC Who Redeveloped SCC After 2 Years of Cancer-Free Survival*

<table>
<thead>
<tr>
<th>Pt No/Age, yr/sex</th>
<th>Stage at Dx</th>
<th>Initial Therapy</th>
<th>Chest RT</th>
<th>Cancer-Free Interval, yr</th>
<th>PS at Relapse</th>
<th>Treatment at Relapse</th>
<th>Survival From Relapse, mo</th>
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<tbody>
<tr>
<td>1/69/M</td>
<td>LTD</td>
<td>CAV</td>
<td>Yes</td>
<td>12.2</td>
<td>3</td>
<td>EP(x4) cycles</td>
<td>NE 4</td>
</tr>
<tr>
<td>2/57/M</td>
<td>EXT</td>
<td>CMC/VAP</td>
<td>Yes</td>
<td>6.2</td>
<td>3</td>
<td>None</td>
<td>2</td>
</tr>
<tr>
<td>3/60/M</td>
<td>EXT</td>
<td>CMC/VAP</td>
<td>No</td>
<td>5.0</td>
<td>5</td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>4/60/M</td>
<td>LTD</td>
<td>CMC/VAP</td>
<td>Yes</td>
<td>5.9</td>
<td>0</td>
<td>None</td>
<td>2</td>
</tr>
<tr>
<td>5/65/F</td>
<td>LTD</td>
<td>CAV</td>
<td>Yes</td>
<td>5.8</td>
<td>3</td>
<td>CAV(x2) cycles</td>
<td>NR 4</td>
</tr>
<tr>
<td>6/63/F</td>
<td>EXT</td>
<td>CMC/VAP</td>
<td>No</td>
<td>5.5</td>
<td>0</td>
<td>EP(x6) cycles+chest RT</td>
<td>CR 46</td>
</tr>
<tr>
<td>7/60/F</td>
<td>LTD</td>
<td>EP</td>
<td>Yes</td>
<td>5.4</td>
<td>2</td>
<td>Carbo(E^{28}) (x3) cycles</td>
<td>PR 4</td>
</tr>
<tr>
<td>8/35/F</td>
<td>EXT</td>
<td>CAPO</td>
<td>Yes</td>
<td>5.0</td>
<td>1</td>
<td>CMC(x1) cycle</td>
<td>NR 7</td>
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<tr>
<td>9/60/M</td>
<td>LTD</td>
<td>CMC/VAP</td>
<td>Yes</td>
<td>4.5</td>
<td>1</td>
<td>CMC(x4) cycles +</td>
<td>CR 26</td>
</tr>
<tr>
<td>10/62/F</td>
<td>LTD</td>
<td>EP</td>
<td>Yes</td>
<td>3.5</td>
<td>0</td>
<td>Anti-GRP+EP(x6) cycles</td>
<td>CR 14</td>
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<tr>
<td>11/52/F</td>
<td>LTD</td>
<td>CAV</td>
<td>Yes</td>
<td>3.4</td>
<td>4</td>
<td>CAV(x1) cycle</td>
<td>NR 1</td>
</tr>
<tr>
<td>12/50/M</td>
<td>LTD</td>
<td>CMC/VAP</td>
<td>Yes</td>
<td>3.0</td>
<td>0</td>
<td>Lobectomy</td>
<td>PR 14</td>
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<tr>
<td>13/66/F</td>
<td>LTD</td>
<td>EP</td>
<td>Yes</td>
<td>3.0</td>
<td>2</td>
<td>Abdomen RT 40 Gy</td>
<td>NR 7</td>
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<tr>
<td>14/57/M</td>
<td>LTD</td>
<td>CAPO</td>
<td>No</td>
<td>2.6</td>
<td>1</td>
<td>CMC(x2) cycles +</td>
<td>CM(x8) cycles</td>
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<tr>
<td>15/60/M</td>
<td>LTD</td>
<td>EP</td>
<td>Yes</td>
<td>2.6</td>
<td>2</td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>16/40/M</td>
<td>LTD</td>
<td>CAV</td>
<td>Yes</td>
<td>2.5</td>
<td>2</td>
<td>CAV(x5) cyclesNR</td>
<td>4</td>
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<tr>
<td>17/37/F</td>
<td>LTD</td>
<td>CAV</td>
<td>Yes</td>
<td>2.3</td>
<td>2</td>
<td>CAV(x4) cycles</td>
<td>PR 4</td>
</tr>
<tr>
<td>18/55/M</td>
<td>LTD</td>
<td>CMC/VAP</td>
<td>No</td>
<td>2.1</td>
<td>1</td>
<td>E(x4) cycles+chest RT</td>
<td>NR 1</td>
</tr>
<tr>
<td>19/42/M</td>
<td>LTD</td>
<td>EP</td>
<td>Yes</td>
<td>2.1</td>
<td>1</td>
<td>EP(x4) cycles+C/Carbo</td>
<td>PR 7</td>
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<tr>
<td>20/50/F</td>
<td>LTD</td>
<td>EP</td>
<td>Yes</td>
<td>2.0</td>
<td>1</td>
<td>EP(x6) cycles</td>
<td>PR 15</td>
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</tbody>
</table>

*Pt=patient; Dx=diagnosis; RT=radiation therapy; PS=performance status; LTD=limited; EXT=extensive; CAV=cyclophosphamide, doxorubicin, vincristine; Carbo=carboplatin; I=ifosfamide; GRP=gastro-releasing peptide; NE=not evaluable; CR=complete response; PR=partial response; NR=no response.

1. Cisplatin, 75 mg/m\(^2\) day 1/etoposide, 100 mg/m\(^2\) day 1 to 3 every 21 days.
2. Cyclophosphamide, 1 g/m\(^2\) day 1/doxorubicin, 40 mg/m\(^2\) day 1/vincristine, 2 mg day 1 every 21 days.
3. Cisplatin, 80 mg/m\(^2\) day 1/etoposide, 80 mg/m\(^2\) day 1 to 3 every 21 days.
4. Carboplatin, 300 mg/m\(^2\) day 1/etoposide, 100 mg/m\(^2\) day 1 to 3 every 21 days.
5. Cyclophosphamide, 1 g/m\(^2\) day 1/methotrexate, 15 mg/m\(^2\) po x 4 doses/lomustine (CCNU), 100 mg/m\(^2\) po day 1 every 6 weeks.
6. Ifosfamide, 240 mg/m\(^2\) day 1,3,5/etoposide, 125 mg/m\(^2\) day 1,3,5, every 21 days.
7. Cyclophosphamide, 500 mg/m\(^2\) day 1/methotrexate, 10 mg/m\(^2\) po x 4 doses every 21 days.
8. Etoposide, 250 mg/m\(^2\) day 1 to 3.
9. Cyclophosphamide, 750 mg/m\(^2\) day 1/carboplatin, 150 mg/m\(^2\) day 1/etoposide, 80 mg/m\(^2\) day 1 to 3 every 21 days.

Evidence of SCC at postmortem examination. Patient 4 redeveloped SCLC in the contralateral lung without evidence of recurrence in the original site 5.9 years after the start of treatment.

Patient Treatment at the Time of Redevelopment of SCC

Patients were treated with a variety of regimens and modalities after redevelopment of SCC (Table 1). The median duration from the time of diagnosis of redevelopment of SCLC to the start of retreatment was 4.9 days (range, 0 to 22 days). Sixteen of the 20 patients (80%) were retreated at the time of redevelopment of disease while 4 were not. Eleven patients were retreated with chemotherapy alone, one with abdominal radiotherapy alone, and two patients with combined chemotherapy and chest radiotherapy. One patient underwent a lobectomy after redevelopment of cancer with both diagnostic and therapeutic intent. An additional patient was treated with a monoclonal antibody directed against the autocrine growth factor, gastrin-releasing peptide, as previously described.29 Four patients received no further antitumor therapy; one patient had relapse documented at postmortem examination, one patient had performance status 3 and did not receive retreatment, and two patients with performance status less than 2 declined further treatment (Table 1).

Nine of the 16 patients (56%) who received treatment at the time of redevelopment of SCC had an objective tumor response: 3 complete and 6 partial. Seven of 13 patients (57%) who received chemotherapy with or without radiotherapy responded (2 complete and 5 partial). The patient treated with the monoclonal antibody directed against gastrin-releasing peptide also achieved a complete response. This patient subsequently received 6 cycles of EP chemotherapy that maintained a response for 10 months.
We also analyzed patients with performance status 0 to 2 at the time of redevelopment of SCLC because these criteria are typically used as entry requirements for clinical trials for patients with newly diagnosed SCLC.\textsuperscript{10,13,18} Among these patients with a performance status of 0 to 2 who received retreatment, 9 of 13 (69\%) had a partial or complete response to therapy. None of the patients whose performance status was greater than 2 had an objective tumor response following retreatment.

Ten patients were treated with a chemotherapy regimen at the time of redevelopment of SCLC which contained one or more drugs that they had received previously (Table 1). Six of these 10 patients (60\%) responded to retreatment. Six patients were treated with the identical chemotherapy regimen at the time of redevelopment of SCLC which they had received at the time of initial diagnosis and three of these patients had a partial response. Eight patients were treated with an etoposide-containing regimen with or without cisplatin at redevelopment of SCLC and 6 of 8 (75\%) responded (2 complete response, 4 partial response). Three of the 8 patients (35\%) not retreated with an etoposide-based regimen had a response (3 partial response).

The median survival after redevelopment of SCC of all 20 patients, including those who did not receive retreatment, was 3.9 months (range, 0 to 46 months) (Fig 1). Six of the 20 patients (30\%) survived more than 1 year from the time of redevelopment of SCLC, and 2 patients (10\%) survived more than 2 years beyond the date of redevelopment. One of these 2 patients died from recurrent SCLC 26 months after treatment at relapse and the other patient remained without evidence of SCLC at the time of her death from bacterial peritonitis 46 months later (Fig 2).

The median survival from the time of redevelopment of SCLC of the 16 patients who were retreated was 6.5 months (range, 1 to 46 months). Analysis of survival based on patient response reveals that the median survival of the 3 patients who achieved complete response was 26 months; the median survival of the 6 patients who achieved partial response was 10 months; and the median survival of those 7 patients who had no response to retreatment was 4 months.

The median survival of the 13 patients who received chemotherapy with or without radiotherapy was 4.4 months (range, 1 to 46 months). The median survival of the 15 patients with performance status 0 to 2, including three patients who were not retreated, was 7.2 months.

Analysis of patients based on the retreatment regimen received shows that the 8 patients retreated with etoposide-based chemotherapy had a median survival of 11 months and the 8 patients who received non-etoposide-based treatment (including radiation and surgery) had a median survival of 5.5 months (p=0.056).

Seven of 13 patients (54\%) who received chemotherapy developed grade 4 or 5 leukopenia from induction therapy at the time of redevelopment of SCLC. Two of the 13 patients (15\%) who underwent retreatment died from infections that were directly related to treatment-induced neutropenia. Six of the 7 patients (86\%) who developed grade 4 or 5 hematologic toxicity during retreatment had received combined modality therapy during their initial treatment of SCLC. Two patients developed grade 3 leukopenia during retreatment and the remaining 4 patients had no hematologic toxicity greater than grade 2. Neutrophil counts were not routinely calculated in all patients.

Sixteen of the 20 patients who redevelope SCC 2 or more years after initial diagnosis died of SCLC. Two patients died from intercurrent infection during the treatment of relapse; one patient died from organic brain syndrome and was found to have SCC in the esophagus at postmortem examination; one patient died from peritonitis 46 months after relapse and had no evidence of SCLC at autopsy.

\section*{Discussion}

Patients who have had late redevelopment of SCC (>2 years from initial diagnosis) can respond to retreatment with chemotherapy and prolonged survival can be achieved. The median survival duration of 7.2 months after redevelopment of SCC in patients with performance status 0 to 2 is approaching that of patients with extensive-stage SCLC and similar functional capacity when measured from the time of initial therapy.\textsuperscript{13,18} The 1-year and 2-year survival probabilities of 30\% and 10\% in our population of patients who redeveloped SCLC is similar to the 1- and 2-year survival
probabilities for initially treated patients with both limited- and extensive-stage SCLC.\(^1\)\(^2\)

It has been suggested previously that the duration of first response to chemotherapy for SCLC is a predictor of the outcome of retreatment at the time of relapse.\(^9\) We have examined the Southwest Oncology Group (SWOG) experience in retreating 67 patients with SCLC who suffered relapses or progressed within a median time of 6 weeks (range, 3 to 28 weeks) from the completion of induction chemotherapy. Forty-six of 67 patients (69%) were initially treated with regimens containing EP, and 21 (31%) were treated with other chemotherapy regimens. Twenty-seven patients (39%) were initially treated with combination chemotherapy and chest radiotherapy. Only 3 of the 67 (4%) patients retreated with cyclophosphamide-based chemotherapy at the time of relapse in this study achieved an objective response. The median survival from the start of retreatment for this group was 10 weeks.\(^8\) The patients were in poor physical condition because nearly half of the patients (46%) in the SWOG study had a performance status of 2 to 4 at the time of relapse. A European Organization for Research and Treatment of Cancer (EORTC) study also examined the outcome of 18 patients with performance status 0 to 3 who suffered relapses with SCLC after a median initial response of less than 34 weeks following treatment with cyclophosphamide, doxorubicin, and etoposide. In this study, 8 of 18 patients (44%) had an objective response to retreatment with cyclophosphamide, doxorubicin, and etoposide and the median survival from the start of retreatment was 17 weeks.\(^9\) Comparison of these three treatment groups is difficult given the differences in performance status and treatment regimens in each
group. Although the response rate in our retreated patients is higher than the response rate in the SWOG cohort (NCI 56% vs SWOG 4%; p<0.0001), it is not significantly different than the EORTC cohort (NCI 56% vs EORTC 44%; p=0.73). The median survival in each group of retreated patients does not appear to be significantly different (NCI 6.7 months vs SWOG 2.5 months vs EORTC 4.2 months). A direct statistical comparison of the survival duration of these three cohorts cannot be done since we have extracted the SWOG and EORTC results from published articles and the individual patient data from these studies are not available.8,9

The objective tumor response after retreatment of late redevelopment of SCLC with agents previously utilized during initial therapy is similar to the experience in salvage therapy of Hodgkin’s disease.30 Fourteen of 19 patients (74%) with Hodgkin’s disease described by Longo et al9 who suffered relapses greater than 1 year from initial diagnosis responded to the identical chemotherapy regimen they had received during initial treatment. The survival duration in these patients was significantly longer than the survival duration of patients with Hodgkin’s disease who suffered relapses less than 1 year from initial diagnosis.30 Similarly, in patients with SCLC who have redeveloped their disease more than 2 years from initial diagnosis, 7 of 13 patients (54%) who were retreated with chemotherapy achieved a partial or complete response. The median survival of 7.2 months among the patients with good performance status who redeveloped SCLC demonstrates that prolonged survival can be achieved in those patients who can tolerate the treatment. Our experience in retreating patients with late redevelopment of SCC is similar to the experience in retreating late relapses of breast cancer and multiple myeloma, in which prolonged survival has also been reported following retreatment.31,32

The hematologic toxicity of salvage chemotherapy in patients who have had late redevelopment of SCLC is significant. Grade 4 or 5 leukopenia occurred in 7 of the 13 patients (54%) who we have retreated with chemotherapy more than 2 years from initial diagnosis. This incidence of myelotoxicity is higher than what was seen in a recent SWOG trial of relapsed patients with SCLC who were retreated within a median of 6 weeks from prior chemotherapy. In the SWOG study, 20 of 67 patients (30%) retreated with cyclophosphamide/cytarabine/vincristine after early relapse developed grade 4 neutropenia. Twenty-six of the 67 patients (39%) in the SWOG study had received prior combined chest radiotherapy and chemotherapy.5 Ten of the 13 patients (77%) we have retreated with chemotherapy at the time of redevelopment of SCC had previously received combined modality therapy. The higher proportion of patients treated with combined chemotherapy and chest radiotherapy may account for the higher incidence of hematologic toxicity we have seen in our patients compared with the patients described by SWOG. For further comparison, in our most recently completed trial of standard-dose EP for patients with newly diagnosed extensive-stage SCLC, initial induction chemotherapy produced grade 4 leukopenia in only 1 of 46 patients (2%).17 Combined modality therapy for SCLC causes increased bone marrow toxicity.15 Therefore, it is not surprising for these patients to develop severe hematologic toxic reactions at the time of retreatment, even 2 years following initial therapy. Although patients with late redevelopment of their SCC may continue to have disease that responds to chemotherapy, their ability to tolerate conventional doses of chemotherapy is likely reduced, particularly those patients who have previously received combined modality therapy.

Two-year survivors of SCLC who redevelop SCLC appear to respond to repeated administration of chemotherapy at a higher rate than patients with earlier redevelopment of the disease. As seen in patients with Hodgkin’s disease, the tumor response to retreatment in patients with late redevelopment of SCC is generally less impressive and shorter in duration than the initial response to therapy at first diagnosis. The short median survival in patients who redevelop SCLC is most likely because the disease is more often recurrent rather than a second primary cancer. We have previously shown that the 18 patients who developed recurrent SCLC followed a typical pattern of recurrence.3 Seven re-presented with cancer in the initial lobe plus regional lymph nodes, five in the initially involved lymph nodes plus distant sites, and six in distant sites alone. We believe that the recurrence of SCLC represents a regrowth of residual SCLC cells that took place after chemotherapy was discontinued. We hypothesize that the regrowth of the tumor over this period of time has allowed a redevelopment of tumor heterogeneity so a significant proportion of the SCLC cells are once again sensitive to readministration of combination chemotherapy. Therefore, many of our patients have had a tumor response after retreatment.

The data presented herein and the data from the literature allow us to make the following recommendations: patients with a performance status of 0 to 2 who redevelop SCLC 2 or more years after initial treatment should be retreated with combination chemotherapy. Certain patients, especially those previously treated with combined modality therapy, are likely to develop grade 3 and 4 hematologic toxic reactions. Therefore, we recommend that physicians initially use chemotherapy regimens that are unlikely to cause severe hematologic toxicity.
REFERENCES