Review article

Treatment of small cell lung cancer patients

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Summary

Small cell lung cancers, comprising approximately 20% of lung cancers, are rapidly growing and disseminating carcinomas which are initially chemosensitive but acquire drug resistance during the course of disease. Thus, outcome is poor with median survival of 10–16 months for patients with limited and 7–11 months for patients with extensive disease. Polychemotherapy with established drugs (platin, etoposide, anthracyclines, cyclophosphamide, ifosfamide and Vinca alkaloids) plays the major role in the treatment of this disease and results in overall response rates between 80%–95% for limited disease and 60%–80% for extensive disease. Dose-intensified chemotherapy and high-dose chemotherapy with peripheral blood progenitor cell support were tested in several trials but their exact impact on outcome remains to be determined. New drugs including the taxanes (paclitaxel, docetaxel), the topoisomerase I inhibitors (topotecan, irinotecan), vinorelbine and gemcitabine are currently evaluated in clinical trials. In limited disease, thoracic radiotherapy improves survival and prophylactic cranial irradiation should be administered to those with a reasonable chance of cure.

Key words: chemotherapy, new drugs, radiotherapy, small cell lung cancer

Introduction

Small cell lung cancers (SCLC) are characterised by rapid growth, early dissemination and development of drug resistance during the course of disease. Therefore, survival is short with median durations of 10 to 16 months for patients with limited and 7 to 11 months for those with extensive disease (Table 1).

The cornerstone of treatment is polychemotherapy. In limited disease, thoracic radiotherapy and in patients with complete remission after induction therapy also prophylactic cranial irradiation should be added to polychemotherapy.

Here we review the current status of polychemotherapy, combined treatment modalities, dose intensity and new drugs in the treatment of SCLC patients.

Table 1: Survival of small cell lung cancer patients (1).

| Survival | Median (months) | 5-year (%)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Polychemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited disease</td>
<td>10–14</td>
<td>2–8</td>
</tr>
<tr>
<td>Extensive disease</td>
<td>7–11</td>
<td>0–1</td>
</tr>
<tr>
<td>Polychemotherapy + local radiotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited disease</td>
<td>12–16</td>
<td>6–12</td>
</tr>
<tr>
<td>Extensive disease</td>
<td>7–11</td>
<td>0–1</td>
</tr>
</tbody>
</table>

Standard chemotherapy

Chemotherapy prolongs survival in patients with SCLC [2]. Currently, patients receive induction chemotherapy with four to six cycles of polychemotherapy. A number of different chemotherapy protocols have demonstrated activity against SCLC [2]. They include cyclophosphamide/doxorubicin/vincristine (CAV), cyclophosphamide/doxorubicin/etoposide (CAE), cyclophosphamide/doxorubicin/vincristine/etoposide (CAVE) and cisplatin/etoposide (PE). These protocols result in overall response rates of 80%–95% in patients with limited disease and 60%–80% in those with extensive disease [2].

A widely used chemotherapy protocol is the combination of cisplatin/etoposide. The response rate of this protocol in extensive disease was marginally better in comparison to the combination of cyclophosphamide/doxorubicin/vincristine [3]. An advantage of cisplatin/etoposide is the fact that this protocol is readily combined with thoracic radiotherapy in patients with limited disease.

In order to obtain optimal activity by non-cross-resistant drugs, the alternating use of cisplatin/etoposide and cyclophosphamide/doxorubicin/vincristine was studied. Some randomised studies reported a higher response rate of the alternating protocol as compared to cyclophosphamide/doxorubicin/vincristine alone [4, 5], but other randomised studies showed no survival advantage for the alternating protocol [3, 6].

Carboplatin has activity similar to cisplatin but is usually better tolerated and easier to administer. Calculation of the
carboplatin dose by means of the Calvert formula [7] appears to relate more closely to both therapeutic and toxic effects of the drug than do doses calculated on the basis of body surface area. In a phase III trial performed by the Hellenic Co-operative Oncology Group [8], carboplatin/etoposide showed equal efficacy but less toxicity in comparison to cisplatin/etoposide in patients with limited disease. A recent trial in elderly patients with limited disease demonstrated promising long-term results by the use of carboplatin/etoposide and local radiotherapy [9].

Several investigators have tried to identify chemotherapy regimens with low toxicity but maximum palliation in patients with poor prognosis. Because of its tolerability and easy administration in an outpatient setting, oral etoposide has been considered a useful treatment for this patient population [10]. In randomised trials in elderly and unfit SCLC patients with extensive disease, however, single agent oral etoposide was less effective both with regard to response rate and quality of life than standard combination chemotherapy with cyclophosphamide/doxorubicin/vincristine or cisplatin/etoposide [11, 12].

Chemotherapy-induced tumour regression primarily occurs within the first cycles of chemotherapy. Consistent with this, randomised trials evaluating the benefit of maintenance chemotherapy failed to significantly improve survival [13, 14], although the recent study by Sculier et al. [15] concluded that maintenance chemotherapy is beneficial in patients responding to induction chemotherapy. Maintenance chemotherapy might produce more toxicity and thus negatively impact on the quality of life.

Combined treatment modalities in patients with limited disease

Chemoradiotherapy

The recognition that local failure is a frequent problem resulted in the inclusion of thoracic radiotherapy in the management of patients with limited disease. A recent meta-analysis of 13 trials demonstrated that the combination of chemotherapy and thoracic radiotherapy is more effective than chemotherapy alone in patients with limited disease [16]. The 3-year survival rate was increased from 8.9% for patients receiving chemotherapy alone to 14.3% for patients receiving chemoradiotherapy. Another meta-analysis [17] confirmed the significant improvement in survival in patients receiving the combined treatment. Thus thoracic radiotherapy should be included in the treatment of patients with limited disease.

Further improvements in radiotherapy are required and possible ways to achieve this include timing and scheduling of radiotherapy as well as increase in dose intensity.

Timing and scheduling of thoracic radiotherapy might be important. Because the primary tumour is the most heterogeneous portion of the total tumour burden [18], it is the most probable site for the development of drug-resistant tumour cells which will then continue to proliferate and metastasise to distant sites. In order to avoid the development of drug-resistant tumour cells at the primary site, thoracic radiotherapy at an early time point during treatment might be advantageous. Consistent with this hypothesis, a meta-analysis including 2440 patients demonstrated superior long-term survival for early administration of thoracic radiotherapy as compared to late radiotherapy [19].

Based on promising observations [20], chemotherapy alternating with radiotherapy was studied. An early trial demonstrated a high complete remission rate using alternating chemoradiotherapy [21]. Nevertheless, recent randomised trials comparing alternating versus sequential chemoradiotherapy in limited disease patients failed to show a significant advantage for the alternating treatment [22, 23].

Another approach to improve the effectiveness of local radiotherapy is to increase the dose intensity of radiotherapy by delivering the daily radiation dose in more than one fraction. Twice-daily radiation therapy, given concurrently with the first of four cycles of cisplatin/etoposide, resulted in improved survival but also more severe esophagitis [24]. A recent randomised study by Turrisi et al. [25] revealed both a significantly improved 5-year survival rate and a reduction of the local failure rate by the use of twice-daily radiotherapy in combination with cisplatin/etoposide as compared to the once-daily schedule.

Table 2 summarises the results of several trials using chemotherapy combined with various schedules of thoracic radiotherapy.

Surgery

While the role of radiotherapy in patients with limited SCLC is well defined, a formal proof of the value of surgical resection is still lacking, except in the rare stage I patients. Several phase II studies of surgery followed by chemotherapy have been published [30–33]. However, the only randomised study by Lad et al. [34] failed to show improved survival for additional surgery in node-positive patients. However, resection was performed rather late (after five cycles of induction chemotherapy) in this study, despite evidence suggesting that local treatment should be given early [18]. Considering the welldocumented favourable results of additional surgery in stage I-III in a recent phase II trial [35], additional studies are warranted.

Prophylactic cranial irradiation

Although brain metastases occur in 50%–80% of patients after two years and are thus a common site of failure [2], the discussion of the role of prophylactic cranial irradiation is still ongoing. Several randomised studies did not definitely establish a beneficial effect of prophylactic cranial irradiation in terms of improving overall survival [36–39], and side effects on brain function remain of concern. However, recent studies of SCLC patients revealed neuropsychiatric abnormalities in 30–40% of SCLC patients even prior to prophylactic cranial irradiation and no consistent further deterioration following this treatment [40–42].
Table 2. Chemotherapy and various schedules of chest radiotherapy in limited disease small cell lung cancer.

<table>
<thead>
<tr>
<th>Literature</th>
<th>Number of pts</th>
<th>Chemotherapy</th>
<th>Time of radiotherapy</th>
<th>CR (%)</th>
<th>Median survival (months)</th>
<th>5-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCracken et al. (26)</td>
<td>154</td>
<td>PEV/CAEM</td>
<td>early concurrent</td>
<td>56</td>
<td>17.5</td>
<td>30*</td>
</tr>
<tr>
<td>Johnson et al. (24)</td>
<td>54</td>
<td>PE</td>
<td>early concurrent</td>
<td>74</td>
<td>21.3</td>
<td>19</td>
</tr>
<tr>
<td>Murray et al. (18)</td>
<td>155</td>
<td>CAV/PE</td>
<td>early concurrent</td>
<td>64</td>
<td>21.2</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>153</td>
<td>CAV/PE</td>
<td>late concurrent</td>
<td>56</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Perry et al. (27)</td>
<td>121</td>
<td>CEV/dox</td>
<td>initial concurrent</td>
<td>49</td>
<td>13.1</td>
<td>7*</td>
</tr>
<tr>
<td></td>
<td>141</td>
<td>CEV/dox</td>
<td>late concurrent</td>
<td>58</td>
<td>14.6</td>
<td>13*</td>
</tr>
<tr>
<td>Takada et al. (28)</td>
<td>114</td>
<td>PE</td>
<td>early concurrent</td>
<td>37</td>
<td>31.3</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>114</td>
<td>PE</td>
<td>late sequential</td>
<td>29</td>
<td>20.8</td>
<td></td>
</tr>
<tr>
<td>Jeremic et al. (29)</td>
<td>52</td>
<td>Carbo/E</td>
<td>early concurrent</td>
<td>96</td>
<td>34</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>51</td>
<td>Carbo/E</td>
<td>delayed concurrent</td>
<td>82</td>
<td>26</td>
<td>15</td>
</tr>
<tr>
<td>Turrisi et al. (25)</td>
<td>206</td>
<td>PE</td>
<td>initial concurrent</td>
<td>87</td>
<td>18.6</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>211</td>
<td>PE</td>
<td>initial concurrent</td>
<td>87</td>
<td>22</td>
<td>26</td>
</tr>
</tbody>
</table>

CR complete remission rate
PEV cisplatin, etoposide, vincristine
CAEM cyclophosphamide, doxorubicin, etoposide, methotrexate
PE cisplatin, etoposide
CAV cyclophosphamide, doxorubicin, vincristine
CEV cyclophosphamide, etoposide, vincristine
Dox doxorubicin
Carbo carboplatin
Concurr. concurrent

A recent meta-analysis including 987 patients demonstrated a 16% reduction in mortality and an absolute 5.4% increase in the three-year survival rate in favour of prophylactic cranial irradiation [43]. Thus this prophylaxis should be administered to patients with limited disease in complete remission after induction chemotherapy.

**Dose intensification of chemotherapy**

*Dose-intensified chemotherapy without peripheral blood progenitor cell support*

Preclinical models have demonstrated a strong relationship between drug dose and tumour cell response with a steep dose-response curve for the majority of anticancer drugs. These studies have indicated that a two-fold increase in dose can result in a ten-fold increase in tumour cell kill [44, 45]. Dose-intensive regimens should result in both reduced tumour regrowth between treatments and potential reversal of drug resistance, thereby more frequently leading to long-term survival.

Intensification of chemotherapy can be achieved by several ways including increase of the initial drug doses, use of hematopoietic growth factors, weekly chemotherapy and shortening of the treatment interval.

A meta-analysis of outcome in patients with limited and extensive disease treated with dose-intensity variations of cyclophosphamide/doxorubicin/vincristine, cisplatin/ etoposide and cyclophosphamide/doxorubicin/vincristine/ etoposide showed no consistent evidence for either higher response rates or longer survival for more intensive regimens [46].

Another approach of dose intensification is to increase drug doses during the initial cycle of chemotherapy. A randomised study in patients with limited disease revealed an improved...
disease-free and overall survival for higher initial doses of cisplatin and cyclophosphamide as compared to lower doses of both drugs [47]. This beneficial effect was achieved despite the fact that dose intensification was very modest and only applied during the first cycle.

The use of hematopoietic growth factors raises the possibility of potentially increasing dose intensity of chemotherapy without excessive myelosuppression. In a randomised trial of weekly chemotherapy with and without hematopoietic growth factors, no increase in received dose intensity could be obtained when the regimen included cisplatin [48] because side effects other than hematotoxicity prevented an increase of dose intensity. Therefore, no improvement in outcome was observed in patients receiving hematopoietic growth factors. A non-cisplatin-containing regimen that resulted in increased dose intensity using hematopoietic growth factors has recently indicated improved survival [49]. In another trial, patients randomised to receive hematopoietic growth factors had a better 2-year survival although no difference in median survival was observed [50]. Dose intensity can only be increased up to approximately 2-fold by the use of hematopoietic growth factors and this increase is not likely to result in a marked prolongation of survival.

With regard to shortening of treatment intervals, a randomised dose intensification study of vincristine/ifosfamide/carboplatin/etoposide with or without hematopoietic growth factors in a 3-week schedule in comparison to a 4-week application showed a significantly improved survival for the shorter interval [51]. Some of the studies on dose-intensity are summarised in Table 3.

High-dose chemotherapy with autologous bone marrow transplantation or peripheral blood progenitor cell support

An early randomised study compared conventional-dose chemotherapy with high-dose intensification plus bone marrow support in responding patients after five cycles of induction chemotherapy (Table 4). High-dose chemotherapy resulted in conversion from partial response to complete response in approximately 75% of the patients. No conversions to complete remission were seen in the responding patients randomised to conventional-dose chemotherapy [52]. Disease-free survival but not overall survival was significantly improved. Because thoracic radiotherapy was not given, the local failure rate was high. In addition, the treatment-associated mortality was high. Thus, the author concluded that high-dose chemotherapy with autologous bone marrow transplantation has no clinically significant advantage.

With improved systemic control by high-dose chemotherapy, loco-regional failures may gain importance. Reasons for this failure are high local tumour burden with high percentage of drug-resistant tumour cells and poor diffusion of anticancer drugs in large tumours. Thus, thoracic radiotherapy should be included in high-dose chemotherapy protocols in the future.

A multimodality phase II trial that included conventional chemotherapy, early high-dose chemotherapy with peripheral blood progenitor cell support, surgical resection, local radiotherapy and prophylactic cranial irradiation led to prolonged disease-free survival in patients with stages I-IIIB [55] (Table 4).

New drugs

The survival statistics clearly indicate the need for new and innovative therapies in order to improve survival. Several new anticancer drugs have become available during the last years. These drugs include the taxanes (paclitaxel, docetaxel), topoisomerase I inhibitors (topotecan, irinotecan), vinorelbine and gemcitabine [56]. The response rates of these drugs as single agents in phase II trials ranged between 26% and 41% in untreated patients with extensive disease [57-61] and are thus similar to those achieved with established drugs (Table 5). Other investigators have explored their role in previously treated patients. These are either 'sensitive' patients, who had responded to first-line therapy and progressed >3 months after their chemotherapy was stopped, or 'refractory' patients, who had failed first-line treatment or relapsed within <3 months after discontinuation of first-line chemotherapy. A

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**Table 3 Dose intensification in small cell lung cancer: recent studies**

<table>
<thead>
<tr>
<th>Literature</th>
<th>Number of pts.</th>
<th>ED (%)</th>
<th>Chemotherapy</th>
<th>Growth factors</th>
<th>Median survival</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woll et al. (50)</td>
<td>65</td>
<td>8</td>
<td>VICE (+ RT)</td>
<td>+ G-CSF</td>
<td>69 wks</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>VICE (+ RT)</td>
<td>- G-CSF</td>
<td>65 wks</td>
<td></td>
</tr>
<tr>
<td>Fukuoka et al. (49)</td>
<td>63</td>
<td>100</td>
<td>CODE</td>
<td>+ G-CSF</td>
<td>59 wks</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CODE</td>
<td>- G-CSF</td>
<td>32 wks</td>
<td></td>
</tr>
<tr>
<td>Steward et al. (51)</td>
<td>300</td>
<td>41</td>
<td>VICE standard</td>
<td>+/- GM-CSF</td>
<td>50 wks</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>VICE intensified</td>
<td>+/- GM-CSF</td>
<td>63 wks</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**ED** extensive disease
**VICE** vincristine, ifosfamide, carboplatin, etoposide
**CODE** cyclophosphamide, vincristine, doxorubicin, etoposide
**NS** not significant

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Table 4. High-dose chemotherapy trials with stem cell support in small cell lung cancer.

<table>
<thead>
<tr>
<th>Literature</th>
<th>Number of pts.</th>
<th>Stage</th>
<th>Chemotherapy</th>
<th>Local therapy</th>
<th>Median survival (months)</th>
<th>2-year DFS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humblet et al. (52)</td>
<td>23</td>
<td>LD, ED</td>
<td>CE, BCNU ABMT</td>
<td>-</td>
<td>17</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>LD, ED</td>
<td>CE, BCNU*</td>
<td>-</td>
<td>13.8</td>
<td>-</td>
</tr>
<tr>
<td>Elias et al. (53)</td>
<td>19</td>
<td>LD</td>
<td>PC, BCNU ABMT</td>
<td>radiotherapy</td>
<td>NR</td>
<td>57</td>
</tr>
<tr>
<td>Perey et al. (54)</td>
<td>67</td>
<td>LD, ED</td>
<td>ICE</td>
<td>-</td>
<td>13.5</td>
<td>-</td>
</tr>
<tr>
<td>Brugger et al. (55)</td>
<td>16</td>
<td>LD</td>
<td>VICE PBPCT</td>
<td>surgery radiotherapy</td>
<td>NR</td>
<td>56</td>
</tr>
</tbody>
</table>

DFS: disease-free survival
LD: limited disease
ED: extensive disease
CE: cyclophosphamide, etoposide
ICE: ifosfamide, carboplatin, etoposide
PC: cisplatin, cyclophosphamide
VICE: vincristine, ifosfamide, carboplatin, etoposide
ABMT: autologous bone marrow transplantation
PBPCT: peripheral blood progenitor cell transplantation
NR: not reached
* conventional dose

Table 5: Efficacy of new drugs as single agents (examples).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of pts.</th>
<th>Stage</th>
<th>Treatment</th>
<th>Overall response (%)</th>
<th>Median survival (months)</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topotecan</td>
<td>48</td>
<td>ED</td>
<td>first-line</td>
<td>39.5</td>
<td>10</td>
<td>Schiller et al. [57]</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>relapsed (sensitive)</td>
<td>first-line</td>
<td>37.8</td>
<td>6.9</td>
<td>Ardizzoni et al. [62]</td>
</tr>
<tr>
<td></td>
<td>47</td>
<td>relapsed (refractory)</td>
<td>first-line</td>
<td>6.4</td>
<td>4.7</td>
<td>Ardizzoni et al. [62]</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>32</td>
<td>ED</td>
<td>first-line</td>
<td>34</td>
<td>10.8</td>
<td>Ettinger et al. [58]</td>
</tr>
<tr>
<td></td>
<td>37</td>
<td>ED</td>
<td>first-line</td>
<td>41</td>
<td>7.3</td>
<td>Kirschling et al. [59]</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>46</td>
<td>ED</td>
<td>first-line</td>
<td>26</td>
<td>9</td>
<td>Burris et al. [60]</td>
</tr>
</tbody>
</table>

ED: extensive disease

phase II study of single-agent topotecan resulted in response rates of 37.8% in 'sensitive' and 6.4% in 'refractory' patients [62]. Interestingly, topotecan appears to have activity toward SCLC brain metastases [63].

A recent randomised study comparing the efficacy of topotecan versus cyclophosphamide/doxorubicin/vincristine in patients with recurrent small cell lung cancer resulted in response rates of 24% for topotecan and 17% for cyclophosphamide/doxorubicin/vincristine [64]. Survival was equal for both treatments. Because topotecan appears to offer better palliation of disease-related symptoms and is also better tolerated, it might be considered as a good choice for second-line chemotherapy.

Because of promising results as single agents, these drugs have been evaluated as part of polychemotherapy protocols. Phase II trials of cisplatin/irinotecan [65] and carboplatin/vinorelbine [66] produced response rates of 83% and 74%, respectively, in patients with limited disease. The combination of paclitaxel/carboplatin/etoposide showed response rates of 93% and 65% in patients with limited and extensive disease, respectively [67]. However, large randomised trials are required to further evaluate the impact of these new drugs as part of polychemotherapy protocols on the outcome of SCLC.

Conclusion

Some progress in combined modality treatment, dose intensification of certain drugs and the development of new chemotherapeutic agents has been achieved. Have these developments an impact on the life expectancy of patients with SCLC?

In extensive disease, the median survival of patients is not so much different from that 20 years ago [68]. This conclusion is based on clinical research data from the US National Cancer Institute (Figure 1 and Table 6). But other workers postulated that a more aggressive approach resulted in an im-
Figure 1. Median survival of small cell lung cancer patients enrolled in various NCI treatment protocols (see Table 6 for details of studies).

Table 6. Median survival of small cell lung cancer patients enrolled in various treatment protocols of the National Cancer Institute.

<table>
<thead>
<tr>
<th>Protocol Number</th>
<th>Reference</th>
<th>Number of pts.</th>
<th>Chemotherapy</th>
<th>Chest radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>73001</td>
<td>Catane et al. (69)</td>
<td>54/32</td>
<td>cyclophosphamide doxorubicin vincristine</td>
<td>concurrent or sequential</td>
</tr>
<tr>
<td>73201</td>
<td>Cohen et al. (70)</td>
<td>6/17</td>
<td>cyclophosphamide methotrexate lomustine</td>
<td>–</td>
</tr>
<tr>
<td>75201</td>
<td>Cohen et al. (71)</td>
<td>19/66</td>
<td>cyclophosphamide methotrexate lomustine vincristine doxorubicin procarbazine with or without etoposide and ifosfamide</td>
<td>–</td>
</tr>
<tr>
<td>77201</td>
<td>Dearing et al. (72)</td>
<td>5/13</td>
<td>see protocol 75201</td>
<td>concurrent, once daily</td>
</tr>
<tr>
<td>77202-0</td>
<td>Bunn et al. (73)</td>
<td>49/0</td>
<td>see protocol 75201</td>
<td>concurrent, once daily</td>
</tr>
<tr>
<td>77202-1</td>
<td>Bunn et al. (73)</td>
<td>48/0</td>
<td>–</td>
<td>–</td>
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<tr>
<td>77204</td>
<td>Brower et al. (74)</td>
<td>0/45</td>
<td>cyclophosphamide doxorubicin etoposide vincristine</td>
<td>–</td>
</tr>
<tr>
<td>80202</td>
<td>Ihde et al. (75)</td>
<td>0/29</td>
<td>Induction: see protocol 75201</td>
<td>–</td>
</tr>
<tr>
<td>83203</td>
<td>Ihde et al. (76)</td>
<td>0/121</td>
<td>Consolidation: cyclophosphamide etoposide followed by ABMT (without consolidation)</td>
<td>radiotherapy to sites of disease</td>
</tr>
<tr>
<td>86204</td>
<td>Johnson et al. (24)</td>
<td>54/0</td>
<td>cisplatin-etoposide</td>
<td>concurrent, twice daily</td>
</tr>
</tbody>
</table>

LD = limited disease  
ED = extensive disease  
ABMT = autologous bone marrow transplantation
proved prognosis [77]. However, recent developments may have some bearing also in advanced disease. The introduction of new drugs active in SCLC and better results with intensified dosing might result in a prolongation of the still disappointing survival of these patients. Thus, further studies in this regard are certainly warranted.

In limited disease, there are more convincing data on improvements over the last two decades. Cisplatin-based protocols plus thoracic radiotherapy resulted in a modest improvement of survival as compared to patients receiving cyclophosphamide-based regimens. Chemotherapy together with early concurrent radiotherapy may result in 5-year survival probabilities of 20% or more. High-dose chemotherapy combined with thoracic radiotherapy might play an increasingly important role in the future. Finally, new drugs with significant antitumour activity have been identified and polychemotherapy protocols that include these new anticancer drugs should be evaluated.

References


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