TABLE 107-10 ADJUVANT CHEMOTHERAPY TRIALS IN NON-SMALL-CELL LUNG CANCER

Trial	Stage	Treatment	No. of Patients	5-Year Survival (%)	*p*
IALT	I–III	Cisplatin-based	932	44.5	< .03
		Control	835	40.4	
BR10	IB–II	Cisplatin + vinorelbine	242	69	.03
		Control	240	54	
ANITA	IB–IIIA	Cisplatin + vinorelbine	407	60	.017
		Control	433	58	
ALPI	I–III	MVP	548	50	.49
		Control	540	45	
BLT	I–III	Cisplatin-based	192	60	.90
		Control	189	58	
CALGB	IB	Carboplatin + paclitaxel	173	59	.10
			171	57	

Abbreviations: ALPI, Adjuvant Lung Cancer Project Italy; ANITA, Adjuvant Navelbine International Trialist Association; BLT, Big Lung Trial; CALGB, Cancer and Lung Cancer Group B; IALT, International Adjuvant Lung Cancer Trial; MVP, mitomycin, vindesine, and cisplatin.

also detrimental in patients with poor performance status (Eastern Cooperative Oncology Group [ECOG] performance status = 2). These data suggest that adjuvant chemotherapy is best applied in patients with resected stage II or III NSCLC. There is no apparent role for adjuvant chemotherapy in patients with resected stage IA or IB NSCLC. A possible exception to the prohibition of adjuvant therapy in this setting is the stage IB patient with a resected lesion ≥4 cm.

As with any treatment recommendation, the risks and benefits of adjuvant chemotherapy should be considered on an individual patient basis. If a decision is made to proceed with adjuvant chemotherapy, in general, treatment should be initiated 6–12 weeks after surgery, assuming the patient has fully recovered, and should be administered for no more than four cycles. Although a cisplatin-based chemotherapy is the preferred treatment regimen, carboplatin can be substituted for cisplatin in patients who are unlikely to tolerate cisplatin for reasons such as reduced renal function, presence of neuropathy, or hearing impairment. No specific chemotherapy regimen is considered optimal in this setting, although platinum plus vinorelbine is most commonly used.

Neoadjuvant chemotherapy, which is the application of chemotherapy administered *before* an attempted surgical resection, has been advocated by some experts on the assumption that such an approach will more effectively extinguish occult micrometastases compared to postoperative chemotherapy. In addition, it is thought that preoperative chemotherapy might render an inoperable lesion resectable. With the exception of superior sulcus tumors, however, the role of neoadjuvant chemotherapy in stage I to III disease is not well defined. However, a meta-analysis of 15 randomized controlled trials involving more than 2300 patients with stage I to III NSCLC suggested there may be a modest 5-year survival benefit (i.e., ~5%) that is virtually identical to the survival benefit achieved with postoperative chemotherapy. Accordingly, neoadjuvant therapy may prove useful in selected cases (see below). A decision to use neoadjuvant chemotherapy should always be made in consultation with an experienced surgeon.

In should be noted that all patients with resected NSCLC are at high risk of recurrence, most of which occurs within 18–24 months of surgery, or developing a second primary lung cancer. Thus, it is reasonable to follow these patients with periodic imaging studies. Given the results of the NLST, periodic CT scans appear to be the most appropriate screening modality. Based on the timing of most recurrences, some guidelines recommend a contrasted chest CT scan every 6 months for the first 3 years after surgery, followed by yearly CT scans of the chest without contrast thereafter.

MANAGEMENT OF STAGE III NSCLC

Management of patients with stage III NSCLC usually requires a combined-modality approach. Patients with stage IIIA disease commonly are stratified into those with "nonbulky" or "bulky" mediastinal lymph node (N2) disease. Although the definition of "bulky" N2 disease varies somewhat in the literature, the usual criteria include the size of a dominant lymph node (i.e., >2–3 cm in short-axis diameter as measured by CT), groupings of multiple smaller lymph nodes, evidence of extracapsular nodal involvement, or involvement of more than two lymph node stations. The distinction between nonbulky and bulky stage IIIA disease is mainly used to select potential candidates for *upfront* surgical resection or for resection after neoadjuvant therapy. Many aspects of therapy of patients with stage III NSCLC remain controversial, and the optimal treatment strategy has not been clearly defined. Moreover, although there are many potential treatment options, none yields a very high probability of cure. Furthermore, because stage III disease is highly heterogeneous, no single treatment approach can be recommended for all patients. Key factors guiding treatment choices include the particular combination of tumor (T) and nodal (N) disease, the ability to achieve a complete surgical resection if indicated, and the patient's overall physical condition and preferences. For example, in carefully selected patients with limited stage IIIA disease where involved mediastinal lymph nodes can be completed resected, initial surgery followed by postoperative chemotherapy (with or without radiation therapy) may be indicated. By contrast, for patients with clinically evident bulky mediastinal lymph node involvement, the standard approach to treatment is concurrent chemoradiotherapy. Nevertheless, in some cases, the latter group of patients may be candidates for surgery following chemoradiotherapy.

Absent and Nonbulky Mediastinal (N2, N3) Lymph Node Disease For the subset of stage IIIA patients initially thought to have clinical stage I or II disease (i.e., pathologic involvement of mediastinal [N2] lymph nodes is *not* detected preoperatively), surgical resection is often the treatment of choice. This is followed by adjuvant chemotherapy in patients with microscopic lymph node involvement in a resection specimen. Postoperative radiation therapy (PORT) may also have a role for those with close or positive surgical margins. Patients with tumors involving the chest wall or proximal airways within 2 cm of the carina with hilar lymph node involvement (but not N2 disease) are classified as having T3N1 stage IIIA disease. They too are best managed with surgical resection, if technically feasible, followed by adjuvant chemotherapy if completely resected. Patients with tumors exceeding 7 cm in size also are now classified as T3 and are consider stage IIIA if tumor has spread to N1 nodes. The appropriate initial management of these patients involves surgical resection when feasible, provided the mediastinal staging is negative, followed by adjuvant chemotherapy for those who achieve complete tumor resection. Patients with T3N0 or T3N1 disease due to the presence of satellite nodules within the same lobe as the primary tumor also are candidates for surgery, as are patients with ipsilateral