Invited Lecture III

The role of adjuvant therapy in completely resected, non-small cell lung cancer

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BACKGROUND

The first well controlled studies of adjuvant therapy in completely resected non-small cell lung cancer (NSCLC) were multicenter trials by the Lung Cancer Study Group in North America (1977-1989). Of the adjuvant agents evaluated (radiotherapy, immunotherapy and chemotherapy), only one study, using adjuvant platinum based chemotherapy, showed a small but significant benefit. This benefit in median survival in stage 2 and 3 completely resected adenocarcinoma was only 7.5 months.

Since then, a large number of randomized controlled trials (RCT's) have been reported, and suggest that some adjuvant chemotherapy regimens may improve survival. Although the reported results have been inconsistent, two meta-analysis reviews undertaken by the Non-Small Cell Lung Cancer Collaborative Group in 1995 suggested that postoperative chemotherapy with platinum based regimens, and in Japan- uracil-tegafur (UFT) regimens were associated with improved survival. A more recent review and meta-analysis by this same group (Sadrakyan et al 2004) reviewed information on 7200 patients enrolled in 19 trials, and concluded that these two regimens of postoperative chemotherapy resulted in a statistically significant improvement in both relative reduction in mortality - and 5 year survival . Benefit was observed in the early stage, node negative patients.

RECENT POSITIVE RANDOMIZED TRIALS

URACIL TEGAFUR (UFT)

The Japanese Lung Cancer Research Group on Postsurgical Adjuvant Chemotherapy reported the results of an RCT to evaluate postoperative, adjuvant oral UFT in completely resected stage 1 adenocarcinoma of the lung (Kato et al 2004). 999 patients entered from 7 surgical centres were enrolled between 1994 and 1997. Median duration of follow up was 73 months. Overall survival was statistically better in the UFT group for T2 lesions, but not for stage T1. An earlier study by the West Japan Study Group for Lung Cancer had shown a similar benefit for this regimen in early stage adenocarcinoma - but no benefit in squamous cell tumours (Tanaka et al 2001). UFT is an oral regimen administered daily for 2 years after operation. The authors report low toxicity (2% grade 3 toxicity - 10 of 482 patients).

ADJUVANT VINOURELBINE AND CISPLATIN (VIN-CIS) IN EARLY STAGE NSCLC

At the annual meeting of the American Society of Clinical Oncology (ASCO), Winton et al reported the results of a randomized trial of adjuvant vinorelbine (VIN) and cisplatin (CIS) in completely resected stage 1B and stage2 NSCLC (ASCO abstract - paper in press). This was a multicentre trial in Canada which recruited 482 patients between 1994 and 2001. Grade 4 hematologic toxicity was common - and febrile neutropenia occurred in 7% - resulting in 2 deaths. Significant non hematologic toxicities occurred in about half of the patients.

Overall survival was significantly prolonged in the VIN-CIS group: 94 months versus 73 months. Five year survival for the VIN-CIS group was 69% compared to 54% for the controls - a significant 15% difference.

FUTURE DIRECTIONS

These recent, positive adjuvant chemotherapy trials are encouraging. Uracil - Tegafur appears attractive in view of the low toxicity. Newer 3rd generation regimens with a cisplatin base may prove less morbid. It is attractive to consider early adjuvant chemotherapy with a cisplatin based drug and add long term oral therapy with UFT.

REFERENCES

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