Survival Not Better With Chemo for Early NSCLC

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ATLANTA — Updated results from a clinical trial that helped establish adjuvant chemotherapy with paclitaxel and carboplatin as the standard of care for stage IB non–small cell lung cancer no longer show a significant improvement in overall survival.

At a median follow-up of 57 months, 5-year overall survival was 59% for adjuvant chemotherapy patients and 57% for those randomized to observation in the Cancer and Leukemia Group B (CALGB) trial known as CALGB 9633. The 2% difference was not statistically significant.

Patients given adjuvant chemotherapy did benefit from significantly improved 2- and 3-year survival in the new analysis. They also had a significantly longer failure-free survival duration, with a hazard ratio of 0.74. Dr. Gary M. Strauss reported the new data on behalf of CALGB at the annual meeting of the American Society of Clinical Oncology (ASCO). Despite some positive effects, CALGB *9633* "can be interpreted as a negative study and, perhaps I should say, should be interpreted as a negative study," he said.

In a shift from his presentation 2 years ago at the same meeting, Dr. Strauss of Brown University, Providence, R.I., said that "the results of CALGB *9633* do not mandate adjuvant chemotherapy as the standard of care in all stage IB patients."

The results do, however, support continued consideration of adjuvant paclitaxel and carboplatin for stage IB patients, in particular, those with tumors 4 cm or more in diameter.

CALGB *9633* had been the only trial among three influential adjuvant therapy studies to report a survival advantage in NSCLC patients with stage IB tumors. At the ASCO meeting 2 years ago, Dr. Strauss reported an 8% improvement in survival with adjuvant chemotherapy (hazard ratio 0.62). A data safety monitoring board closed the trial early because its primary outcome had been reached.

The early stopping was justified but "potentially problematic," Dr. Strauss said. It did not negate the earlier results, but it left the study without sufficient statistical power to detect "smaller differences that are nonetheless clinically significant," he added.

Five-year overall survival was 59% for adjuvant chemotherapy patients and 57% for those randomized to observation; all patients had stage IB disease.

Investigators had already revamped CALGB *9633* from an initial goal of 500 patients to a target of 384 patients because of slow accrual.

After complete resection of their tumors, 171 patients were randomized to observation and 173 patients to four cycles during each of which they received 200 mg/m^2 of paclitaxel and carboplatin AUC 6 for 3 weeks. Chemotherapy was reported to be well tolerated. About a third of patients had grade 3 or 4 neutropenia, but there were no therapy-related deaths.

As of April 19, 2006, the latest data cutoff, median overall survival was 95 months for patients who had received adjuvant chemotherapy and 78 months with observation. Though the hazard ratio was 0.80, the difference was not statistically significant. Overall survival was significantly better for the adjuvant chemotherapy arm at 2 years (90% vs. 84% for the control arm) and at 3 years (79% vs. 71%), but not thereafter.

Failure-free survival favored adjuvant chemotherapy, with a median of 89 months vs. 52 months in the observation arm. The difference was significant at 3 years, when 66% of the adjuvant arm but only 57% of the observation arm had no recurrence.

In an unplanned subset analysis reported by Dr. Strauss, the investigators did find a significant survival benefit for patients whose tumors were 4 cm or larger in diameter (hazard ratio 0.66), but not for those with smaller tumors.

As only 137 of 155 deaths required for final analysis have so far been observed, Dr. Strauss emphasized that the new report is still only a preliminary analysis. In conclusion, he said the significant advantages in 3-year and in disease-free survival suggest that the regimen is effective and may delay recurrence, even if it does not enhance the likelihood of a cure. ■

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