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Weekly alternating non-cross-resistant chemotherapy for small cell lung cancer with a good prognosis: a study of the Hellenic Cooperative Oncology Group.

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Source

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Abstract

This trial was conducted by the Hellenic Cooperative Oncology Group to improve the responses and survival in small cell lung cancer with a good prognosis, using a weekly intensive chemotherapy with alternated non-cross-resistant myelosuppressive agents. Patients were classified into two groups; group A consisted of those who received the initial designed regimen (29 patients), and group B consisted of those who received the more intensified regimen that increased by 25% the doses of carboplatin, epirubicin, and ifosfamide, and by 33% the doses of etoposide given on days 1, 2, and 3 with prophylactic granulocyte colony-stimulating factor support. Chemotherapy in group A consisted of carboplatin 150 mg/m2 in 250 ml of 5% dextrose in water as an 1-hour infusion on day 1, etoposide 75 mg/m2 in 250 ml normal saline as an 1-hour infusion on days 1 and 2 alternating with epirubicin 30 mg/m2 intravenous push on day 8, and ifosfamide 2 g/m2 in 500 ml 5% dextrose in water as a 2-hour infusion with mesna protection on day 8. Responding patients with limited disease were also treated with thoracic irradiation. Those who achieved complete response received prophylactic cranial radiotherapy. In group A, the overall response rate was 79.3%, with a 27.6% complete response rate, a median time to progression of 5.71 months, and a median survival of 8.3 months. For patients with limited disease, the response rate was 75%, with a 40% complete response rate, a median time to progression of 5.87 months, and a median survival of 10.98 months. The respective numbers for extensive disease were 89% (only partial responses), 4.82 months, and 5.67 months. The toxicity was mild and manageable. There were no dose reductions or treatment delays. In view of the excellent tolerability and the rather low efficacy of the initial regimen, we decided to administer the more intensified one with granulocyte colony-stimulating factor support. In Group B, the overall response rate was 91.8%, with a 45.9% complete response rate, a median time to progression of 7.05 months, and a median survival of 10.16 months. For limited disease, the response rate was 93%, with a 52% complete response rate, a median time to progression of 7.05 months, and a median survival of 10.49 months. The respective numbers for extensive disease were 88% (25% complete response), 6.82 months, and 9.02 months. The toxicity of this more intensified regimen was more severe but acceptable. Myelosuppression was the main toxicity. However, grade 3-4 febrile neutropenia requiring hospitalization occurred only in 6% of patients. The relative dose intensity was 91%, probably the result of the prophylactic use of granulocyte colony-stimulating factor. The differences in response rate, time to progression, and survival were not statistically significant between the two groups. There were statistically significant differences in the response rate ($p = 0.019$) and survival rate ($p = 0.001$) between limited disease and extensive disease only in group A. In conclusion, this weekly, alternated regimen, specifically the intensified regimen, appears to be very active and well tolerated in patient who have small cell lung cancer with a good prognosis. However, despite the high efficacy, this study failed to show any survival advantage as compared with that obtained with the standard treatment for small cell lung cancer.