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Randomized comparison of early versus late hyperfractionated thoracic irradiation concurrently with chemotherapy in limited disease small-cell lung cancer: a randomized phase II study of the Hellenic Cooperative Oncology Group (HeCOG).

Skarlos DV, Samantas E, Briassoulis E, Panoussaki E, Pavlidis N, Kalofonos HP, Kardamakis D, Tsiakopoulos E, Kosmidis P, Tsavdaridis D, Tzitzikas J, Tsekeris P, Kouvatseas G, Zamboglou N, Fountzilas G.

Source

Athens Medical Center, Greece. hecogoff@otenet.gr

Abstract

BACKGROUND:

Concurrent platinum etoposide chemotherapy given in combination with hyperfractionated thoracic radiation therapy (HTRT) in limited disease (LD) small cell lung cancer (SCLC) is associated with a high response rate and significant prolongation of survival. Given these results, the Hellenic Cooperative Oncology Group (HeCOG) performed a multicenter randomized phase II study in patients with LD SCLC to evaluate the timing of HTRT (early vs. late) when given concurrently with chemotherapy.

PATIENTS AND METHODS:

To be eligible for the study, patients were required to have histologically or cytologically proven LD SCLC, confined to one hemithorax and/or ipsilateral mediastinal or supraclavicular lymphnodes and absence of pleural effusion or controlateral supraclavicular lymphnode involvement. Moreover, patients had to have a good performance status and adequate haematological, liver and renal function. Patients with LD SCLC were randomized to receive HTRT either concurrently with the first (Group A) or with the fourth (Group B) cycle of chemotherapy. Chemotherapy consisted of carboplatin administered at an AUC of six given as an i.v. 1-hour-infusion immediately followed by etoposide at a dose of 100 mg/m2 i.v. as a two-hour infusion for three consecutive days every three weeks up to a total of six cycles. Prophylactic cranial irradiation was also given to patients achieving a complete response.

RESULTS:

42 and 39 patients, were eligible for efficacy evaluation in group A and B respectively. The overall response rate was 76% in group A and 92.5% in group B (P = 0.07) with a complete response rate of 40.5% and 56.5%, respectively. After a median follow-up of 35 months, time to progression was 9.5 months in group A and 10.5 in group B (NS) while overall median survival was 17.5 and 17 months respectively (NS). The 2-year survival was 36% in group A and 29% in group B (NS) and the 3-year survival 22% and 13%, respectively (NS). The distant relapse rate was 38% in group A and 61% in group B (P = 0.046). Severe grade 3 4 anemia was recorded in 19% of group A and 12.5% of group B (NS), while severe leucopenia was recorded in 35.5% and 20.5% (P = 0.09) and neutropenic fever in 5% and 2.5% (NS), respectively. Severe thrombocytopenia did not differ significantly between the two treatment groups being 21.5% and 23%, respectively. Severe grade 2-3 esophageal toxicity was 19% in group A and 23% in group B (NS), while grade 3 lung toxicity was 5% and 7.5% (NS), respectively. No toxicity-related deaths were recorded.

CONCLUSION:

Concurrent administration of HTRT with carboplatin etoposide is associated with a high response and survival rate. Although a trend for higher response rate was recorded in the group of patients who received late HTRT, the overall median, 2-year and 3-year survival rates did not differ significantly between the two treatment groups. The toxicity of this promising therapeutic approach was acceptable. Comparative phase III studies with an adequate number of patients are recommended in order to answer this question.