Role of Radiaton Therapy in the Combined-Modality Treatment of Patients with Extensive Disease Small-Cell Lung Cancer: A Randomized Study

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Summary

The authors have published a single institution study from the University Hospital in Kragujevac, Yugoslavia. Two hundred ten patients with extensive stage small cell lung cancer (SCLCa) were enrolled onto this prospective trial, which was partially randomized. All those enrolled were treated with 3 initial cycles of cisplatin and etoposide (PE) chemotherapy. Those patients who had a complete response (CR) of their distant disease and either a partial response (PR) or CR of their local disease went on to be randomized to:

- Accelerated hyperfractionated radiation therapy (AHFRT) to the thorax with concurrent carboplatin and etoposide (CE) chemotherapy followed by 2 more cycles of PE chemotherapy
- PE chemotherapy x 4 more cycles alone.Only 109 patients met criteria to be randomized. The other 111 patients were treated prospectively according to a set protocol:
- Those that only had a PR at distant sites of disease (and either a CR or PR at the local site) went on to receive 2 more cycles of PE followed by AHFRT and concurrent CE
- Those that had stable or progressive disease went on to best supportive care or oral VP-16.Prophylactic cranial irradiation was administered if the patient had a CR to treatment

Results

The median survival of those in arm 1 and 2 above were 17 and 11 months, respectively - a statistically significant difference.

Background

Extensive disease SCLCa continues to represent a challenge to the field of oncology. Most patients with extensive disease respond well to treatment, yet the median survivals remain around 10 - 12 months. The 5 year survival rates are under 5% in most reported series.1,2 The standard of care continues to be chemotherapy with a duration of 4 - 6 cycles.3 The benefits of thoracic radiation therapy (TRT) have been demonstrated in numerous randomized trials for limited stage disease. A large intergroup trial has demonstrated that AHFRT over standard fractionation TRT seems to further benefit patients with limited disease SCLCa.4 Most of the literature to date has not demonstrated an advantage in treating extensive disease with TRT in regards to response or survival.

This article has demonstrated that in selected individuals in whom a CR is obtained at the distant sites of disease, AHFRT to the thorax impacts on survival. The 5-year survival rates of patients in arms 1 and 2 were 9.1% and 3.7%, respectively. Survival for the other patients was 0% by 4 years. A higher CR rate at the thoracic primary was shown favoring arm 1 over arm 2. In terms of toxicity, arm 2 had a much higher rate of severe nausea and vomiting, alopecia and renal damage than arm 1. Arm 1, as expected, had more esophageal irritation.

The results of this trial suggest that a certain subset of extensive stage patients may benefit from TRT in regards to survival, as is the case in limited stage SCLCa. However the TRT regimen given as AHFRT is fairly

intensive - twice daily TRT for 18 consecutive days (54 Gy in 1.5 Gy fractions) with concurrent CE. This may not be tolerable for most patients. The future trials may utilize AHFRT for good performance status patients and standardized fractionation for others. A larger scale, multi-institutional confirmatory trial may also be of some benefit.