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Editorial

Palliative Radiotherapy for Lung Cancer: Is it Enough?

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Lung cancer is now the leading cause of cancer deaths in both men and women in the UK. Non-small cell lung cancer (NSCLC) accounts for approximately 80% of all primary lung cancers and approximately two-thirds of patients present with inoperable, advanced disease. The 5-year survival for patients with Stage IIIb disease is approximately 5%; it is 1% for Stage IV patients. Survival rates in the UK are lower than in Europe [1]. This has been attributed to the inadequate provision of appropriate cancer treatment and a lack of appropriately trained cancer specialists.

The article in this issue by Quddus et al. is a retrospective study of treatment of patients with NSCLC who received radiotherapy of ten fractions or fewer and survived for 5 years or more. The surviving patients (61/4531 i.e. 1.3%) were heterogeneous with respect to the initial stage, with 46% staged as I or II; 29% of the total surviving had no histological diagnosis but were assumed to have NSCLC. The survival of 1.3% of the initial cohort at 5 years may have been expected without radiotherapy, although there was evidence of a maintained radiological response in 55%. Long-term survival was more frequent in patients receiving ten-fraction regimens on univariate analysis, but we do not know if this was independent of performance status or stage.

Prognostic factors have been identified that affect the response to radiotherapy and chemotherapy, and also survival, with stage being the most important prognostic factor [3]. Other factors affecting response include performance status, metastatic disease in liver and bone; and the use of combination chemotherapy [4,5]. Poor performance status, pretreatment weight loss, comorbidity and raised serum lactate dehydrogenase levels have been associated with poor survival [6]. Age and histological subtype have not been shown to correlate with response and survival. Poor performance status has been associated with an increased risk of toxicity with chemotherapy and with early death [7,8].

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As discussed in the Quddus et al.'s article in this Journal [2], two Medical Research Council studies have been carried out in this field. A small survival advantage (median 2 months, 5% at 1 year and 3% at 2 years) has been shown for more intensive radiotherapy (39 Gy in 13 fractions, 5 days per week compared with 17 Gy in two fractions 1 week apart) for patients with inoperable NSCLC that is too advanced for potentially curative radiotherapy and who have good performance status (World Health Organization (WHO) 0–2). Patients in the more intensive arm experienced more toxicity and less rapid palliation of symptoms. Previously, a single dose of radiotherapy has been shown effectively to palliate patients with a poor performance status (WHO 3–4) with no impact on survival.

In the last decade there has been increasing interest in the use of multimodality therapy, although, despite increasing evidence for the role of chemotherapy in the palliation of lung cancer, there still remains resistance to its use. The palliative use of chemotherapy is no longer controversial in the United States (ASCO guidelines 1997 [9]). A meta-analysis of 52 randomized trials of chemotherapy in NSCLC demonstrated a survival advantage tor cisplatin-based chemotherapy (hazard ratio 0.73; 27% reduction in risk of death and 10% improvement in survival at 1 year) compared with best supportive care in advanced disease. The addition of chemotherapy to radical radiotherapy for locally advanced disease gave a hazard ratio of 0.87 (13% reduction in the risk of death, absolute benefit of 4% at 2 years) [10,11]. Chemotherapy can palliate symptoms in advanced disease, with symptomatic relief seen after one or two courses [12], and a total of three courses of triple therapy has been shown to be as effective as a prolonged treatment course [13]. Newer cytotoxic agents such as navelbine, gemcitabine, docetaxel and paclitaxel have all been evaluated as single agents compared with chemotherapy and have been shown to palliate symptoms, maintain or improve quality of life, and have a positive effect on survival [14–17].

The current literature would support the role of cisplatin-based chemotherapy for good performance

status, informed patients with inoperable lung cancer (some Stage IIIa, Stage IIIb and Stage IV). With this evidence, it is now necessary to determine the best 'multimodality palliation' with the most effective and best tolerated combination of cytotoxic drugs, the optimum dose of radiotherapy, and have to select those patients with advanced lung cancer who will benefit. The choice of which palliative option to use should not be an 'either/or'; it should be a decision on appropriateness and a relative order of palliative options. We still do not know the role of high-dose palliative radiotherapy with chemotherapy compared with either option alone.

Future advances in the treatment of advanced lung cancer may lie in the development of novel approaches, such as drugs that may suppress tumour angiogenesis, gene therapy and immunotherapy. Renewed interest in screening may also enable patients to be diagnosed at an earlier stage and continued emphasis should be placed on the dangers of smoking. It is to be hoped that the future will see reports on large series of patients treated with palliative chemotherapy with and without radiotherapy, so that we can speculate once again on what contributes to 'cure'.

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