Small Cell Lung Cancer (SCLC); any progress?

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Introduction

In a 2007 report, lung cancer with 334,800 deaths (19.7% of the total cancer deaths) was the most common cause of cancer deaths in Europe [1]. A decrease in the proportion of lung cancer patients with SCLC has occurred in the USA but it still remains 15–20% in Europe. Although over the last 5 years, lung cancer declined by 1.9% per year in men, it has increased by 1.7% in women [2].

Prognostic groups

Treatment

Tumour extent is defined as extensive stage (ES) or limited stage (LS) disease. FDG-PET might improve SCLC CT staging but validation is required. Moreover, there are a number of other independent prognostic factors that predict survival including performance status (PS) and biochemical indices but not age [3]. Recently a Dutch study rather surprisingly found negligible influence of comorbidity on prognosis [4].

Treatment of poorer prognostic groups:

Despite a general view, survival with cisplatin etoposide (PE) regimens either alone or alternating with cyclophosphamide, doxorubicin, vincristine (CAV), was not significantly better in randomised clinical trials (RCTs) than CAV alone for ES patients. The position was, confirmed in a trial of PE and (CEV) cyclophosphamide epirubicin vincristine [5], and by similar comparative trials. However a small statistically significant survival advantage with less hospitalisation was found for paclitaxel carboplatin versus CAV [6].

A Japanese group reported a survival benefit for the combination irinotecan cisplatin over PE but recently the benefit was not confirmed in a western population using a modified weekly regimen [7]. Nevertheless an update of a German trial carboplatin etoposide, CbE +paclitaxel was superior to CbE+ vincristine, 5 year survivals 14% vs. 6% [8]. Although RCTs of gemcitabine carboplatin, irinotecan carboplatin, and oral topotecan cisplatin have not improved survival compared with platinum etoposide. A recent randomised Phase II trial compared pemetrexed with either cisplatin or carboplatin and has led to a global trial (GALES) in ES of pemetrexed carboplatin vs. carboplatin etoposide [9]. Only recently was the superiority of chemotherapy (oral topotecan) over best supportive care demonstrated, [10]. Data on 3rd line therapy reported a median survival of 5 months [11]. There is no optimal treatment as yet for this poorer prognosis group of patients.

Limited stage, good performance status, the better prognosis patients subgroup

Standard chemotherapy includes a variety of platinum containing regimens, recently the Norwegian trial demonstrated survival benefit for PE over CEV in LS patients [5]. In another large trial of better prognosis patients ICE ifosphamide carboplatin etoposide with mid-cycle vincristine demonstrated superior survival over standard CT which included CDE and in some cases PE [12].

A large phase III trial examined a substantial dose intensity (DI) increase using peripheral blood stem cells, increased in the patient's whole blood by G-CSF and then reinfused as autotransfusions. Disappointingly no survival benefit for the DI regimen over standard chemotherapy was observed [13].

Combined modality treatment

Thoracic radiotherapy (TRT)

A recent review reported a 5% 2 year survival increase with early (<9 weeks from start of CT) TRT compared with later TRT, subset analyses suggested a greater survival benefit with platinum based CT and hyperfractionated TRT [14]. However in a repeat of the Canadian NCIC trial, no survival difference was found between early once daily TRT given on cycle 2

and later TRT on cycle 6 of CT [15]. Nevertheless a recent systematic overview has supported the use of early TRT [16]. Comparing twice daily TRT vs. once daily total 66 Gy, concurrent with CT is the concept of the CONVERT trial.

Prophylactic cranial irradiation (PCI)

Two European trials of PCI are investigating PCI at two different schedules in LS patients in complete response and the effect of PCI vs. no PCI in ES patients with a CT response.

Future

Newer forms of radiotherapy and the incorporation of radiotherapy and chemotherapy in combined modality regimens still require further investigation. Novel drugs in current/planned local trials include pemetrexed, amrubicin and a variety of anti angiogenics [17]. These avenues and evaluation of new agents, both chemotherapeutic and biological make the future research of SCLC exciting.

Potential conflict of interest

The authors have received honoraria, and research support from a variety of pharmaceutical companies and non profit organisations. NT has received honoraria and research support Amgen, Bristol Myers Squibb, Chugai, GSK, Eli Lilly. PL has received honoraria from Pharmion FB Educational support, research funding and honoraria from Sanofi-Aventis, Lily, Roche, Astra-Zeneca, AMGEN.

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