A NOVEL PHASE II TRIAL OF IPILIMUMAB, CARBOPLATIN AND ETOPOSIDE (ICE) FOR THE FIRST LINE TREATMENT OF EXTENSIVE STAGE SMALL CELL LUNG CANCER (SCLC)


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Background: Platinum etoposide doublet chemotherapy remains the standard of care for SCLC; newer combination regimens have failed to improve outcome. A subgroup of patients with apparently better long-term survival present with autoimmune paraneoplastic syndromes. These reflect cross reactivity of anti-tumour immune responses with self-antigens, most frequently neuronal antigens, and suggest that SCLC is susceptible to immune control. Our study examines for the first time, whether addition of the immune stimulating anti-CTLA4 antibody Ipilimumab to carboplatin/etoposide chemotherapy can increase anti-tumour activity and whether this might come at the cost of extra immune related neurological toxicity.

Methods: This phase II study examines the efficacy and toxicity of Ipilimumab (10 mg/kg) together with Carboplatin (AUC=6) and Etoposide (120 mg/m2 IV day1, 100mg BD PO days 2 and 3) chemotherapy in previously untreated patients with extensive stage (ES) SCLC. Ipilimumab was introduced in responding patients at cycles 3-6 with planned 3-monthly maintenance Ipilimumab. Primary end point is progression free survival at 1 year; secondary endpoints include 1 year overall survival and Immune related progression free survival (irPFS).

Results: 39 of a planned 40 patients have entered the study with a median age of 58 yrs (range 47-84); 64% are male. Patients received at least one cycle of Ipilimumab. In 61.1% [95% CI: 44.9-75.2] grade 3 adverse events were seen, assessed by the investigators as possibly ipilimumab related in 41.7% [95% CI: 27.1, 57.8]. Two patients (6%) had ipilimumab related neurological events, of these one was fatal, presenting like an anti-Hu syndrome. Both events occurred in patients with positive baseline anti-neuronal antibodies.

Conclusions: Our multi centre study has demonstrates for the first time that chemo-immunotherapy with ICE is deliverable in ES SCLC, but with an appreciable burden of immune related toxicity. Two significant neurological immune mediated events were seen, one fatal. The data reinforce the view that SCLC is immunogenic and that immunological visibility of the tumour can link to anti neuronal immune events.

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