Combination chemotherapy shows benefits for adrenal cancer patients

Posted on Thursday 3rd May 2012

Endocrinologists at the University of Birmingham have played a key role in a major international clinical trial which has found that giving a combination of chemotherapy drugs to patients suffering from advanced adrenal cancer can help them to live up to a fifth longer.

The results of the First International Randomised Trial in Locally Advanced and Metastatic Adrenocortical Carcinoma Treatment (FIRM-ACT), which was conducted at 40 specialist centres in a total of 12 countries and was the largest ever clinical trial into adrenal cancer, are published online today in the *New England Journal of Medicine*.

Adrenocorticol carcinoma is a rare but aggressive cancer, mainly occurring in middle-aged adults. Because of the adrenal glands' location deep in the body, most malignant tumours are not found until they have grown quite large and may already have spread to other organs and vessels via the lymphatic system. Patients usually respond poorly to cytotoxic treatment, with less than 15 per cent surviving for five years among those in whom the disease has spread.

This first phase three trial of treatment compared the two most successful drug regimens in patients with advanced adrenal cancer to try to establish a treatment standard. One combined etoposide, doxorubicin, and cisplatin (EDP) with mitotane. The second combined streptozotocin with mitotane. A total of 304 patients took part in the study between June 2004 and October 2009.

Participants were randomly assigned to receive mitotane plus either etoposide, doxorubicin and cisplatin every four weeks or streptozotocin every three weeks. Patients with disease progression received the alternative regimen as second-line therapy.

Rates of response and progression-free survival were significantly better with EDP plus mitotane than with streptozotocin plus mitotane as first-line therapy, with similar rates of toxic events, although there was no difference in overall survival. The average rate of survival was 14.8 months and 12 months respectively.

The authors conclude: 'EDP plus mitotane as first-line treatment reduced the risk of death by 21 per cent as compared with streptozotocin plus mitotane in the intention-to-treat analysis'.

Professor Wiebke Arlt, Head of the Centre for Endocrinology, Diabetes and Metabolism at the University of Birmingham and UK co-ordinator of CIRM-ACT, comments: 'FIRM-ACT has established the best chemotherapy regimen in adrenocortical cancer. However, the poor overall survival demonstrates that we urgently need even better treatment options for this devastating disease. FIRM-ACT is the largest study ever carried out in patients with adrenal cancer. We were able to recruit a large number of patients in a relatively short time frame.

She adds: 'Importantly, this shows that clinical studies are possible even in very rare cancers, if researchers achieve a successful international collaboration, as was the case in FIRM-ACT. We are currently taking this work forward, supported by European funding, as part of the EU FP7 research network ENSAT-CANCER.

For more information, please contact Jenni Ameghino, Press Officer, University of Birmingham, 0121 415 8134. Mobile: 07768 924156.

Notes to editors

- **The Centre for Endocrinology, Diabetes and Metabolism at the University of Birmingham is recognised as a centre of world-leading excellence in endocrinology. Training the researchers of tomorrow is a major remit of its research strategy. The Centre comprises 19 principal investigators and several groups focus on endocrine cancer and steroid hormone research.**
- **Professor Arlt leads a multi-disciplinary Adrenal Tumour Specialist Service at the nearby Queen Elizabeth Hospital and currently acts as the UK lead for a number of studies in patients with adrenal cancer.**