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Results of international trial show promise in rare, difficult to treat cancer

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Neuroendocrine tumours (NETs) develop in the neuroendocrine system, responsible for producing the hormones that regulate the working of different organs in the body. They are rare, incurable, and treatments for them are limited, especially once they have become advanced. Now an international team of researchers has shown that the use of the mTOR inhibitor, everolimus, can delay tumour growth among both gastrointestinal and lung NETs. This is particularly important for patients with the lung tumours, the researchers say, because there is currently no approved treatment for such cases.

Reporting on the results of the RADIANT-4 trial, a placebo-controlled, double-blind, phase III study carried out in centres in 13 European countries, Korea, Japan, Canada, and the US, Professor James Yao, MD, Chair of the Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA, will tell the 2015 European Cancer Congress today (Sunday) that the treatment had a significant effect in non-functional NETs. Non-functional NETs either do not secret a hormone, or secrete one that does not cause symptoms, and are therefore often diagnosed later when the cancer has become advanced. "About 80% of all NETs are thought to be non-functional, so, unfortunately, late diagnosis is common and poses a major problem for these patients," he will say.

The trial included 302 patients with a median age of 63. After randomisation, 205 received everolimus and 97 placebo. The most common tumour sites were lung (30%) and ileum, the lowest part of the

small intestine (24%). In the everolimus group, 53% had had prior therapy with somatostatin analogue (SSA), chemotherapy (26%), and radiotherapy (22%). SSAs are widely used in NETs to reduce hormone secretion, thus inhibiting tumour growth and reducing symptoms. Although they are effective in gastrointestinal tumours there is as yet no evidence that they delay tumour growth in lung NETs.

In the placebo group the percentages were 56% for SSA treatment, 24% for chemotherapy, and 20% for radiotherapy. "So the groups were well balanced in their prior treatment, and we can be sure that there were no confounding factors in that respect," says Prof Yao.

When progression-free survival (the time during which the patient is alive and the disease does not worsen) was assessed, the investigators found an important difference between the two groups. "We found a statistically significant 52% reduction in the risk of progression or death in favour of everolimus, and also a clinically meaningful 2.8 fold (7.1 months) improvement in median progression free survival compared with those who had taken placebo. In addition, everolimus was well tolerated by the patients and its safety profile was good. We also saw a trend towards an improved overall survival, but the overall survival analysis is an interim one and it is too early to be able to be more definite about this at this time," Prof Yao will say.

"Although we knew from previous studies that everolimus could delay the growth of pancreatic NETs, this is the first time we have been able to conclusively show that it is effective in other NET sites. We hope that our results will provide a new treatment option for lung and gastrointestinal NETs, and we look forward to reporting further results from the trial, including those on final overall survival and quality of life, in the future."

Professor Peter Naredi, the ECCO scientific co-chair of the Congress,

who was not involved in the research, commented: "For clinicians treating patients with neuroendocrine tumours the European Cancer Congress this year is exciting. For these rare cancers we will have two phase III trials reported and both will present positive results from the test treatment. Professor Yao and co-workers have shown that everolimus can be used in the treatment of advanced non-functional NETs of lung and gastrointestinal origin."

Provided by ECCO-the European CanCer Organisation