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Phase III study shows everolimus delays tumor progression in hard-to-treat neuroendocrine tumors

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The results of a large Phase-III clinical trial have shown that the drug everolimus delays tumor progression in patients with a hard-to-treat group of rare cancers that affect particular hormone-producing cells.

At the 35th Congress of the European Society for Medical Oncology (ESMO), Dr Marianne Pavel from Charité University in Berlin, Germany reported that everolimus improved progression-free survival by 5.1 months in patients with advanced neuroendocrine tumors.

Neuroendocrine tumors are slow-growing malignancies that originate from cells of the body's neuroendocrine system. These cells are found throughout the body in organs such as the gastrointestinal tract and the lungs. The tumors are mostly non-responsive to chemotherapy drugs. They affect less than five people in 100,000, and until now there have been few treatment options for inhibition of tumor growth.

In the new RADIANT-2 trial, researchers in several European countries and the USA treated 429 patients with progressing, well- or moderately-differentiated advanced neuroendocrine tumors with either everolimus plus a somatostatin analog called octreotide LAR, or placebo plus octreotide LAR.

All patients had a history of 'carcinoid' symptoms, meaning the tumors have been secreting excessive levels of amines, especially serotonin,

leading to symptoms such as flushing and diarrhea. The tumor originated in the small intestine in about 50% of patients.

Overall, the median progression-free survival for patients given everolimus plus octreotide LAR was 16.4 months, significantly longer than the median 11.3 months for placebo plus octreotide LAR, Dr Pavel reported.

"This is the first Phase-III trial of the combination therapy with octreotide LAR and everolimus and it is the largest trial that has ever been done in this type of neuroendocrine tumors," Dr Pavel said. "When we designed the study, we tested for an improvement of at least 4.5 months compared to octreotide LAR and were pleased with the resulting 5.1 month difference."

Currently, treatment options for neuroendocrine tumors are limited. Chemotherapy is only effective in neuroendocrine tumors affecting the pancreas. For tumors that originate in other organs, treatments include somatostatin analogs that control symptoms related to over-secretion of compounds such as serotonin. Interferon-alpha is also approved for these types of neuroendocrine tumors which are also referred to as carcinoid tumors. A placebo-controlled trial recently demonstrated that octreotide LAR has anti-tumor effects in neuroendocrine tumors of the small intestine.

"Since chemotherapeutic drugs are not effective in this type of neuroendocrine tumor patient, we now have for the first time a drug that has been studied in a Phase-III trial that offers antitumor efficacy in addition to the currently available agents, somatostatin analogs and interferon," Dr Pavel said.

"I think the drug will be further explored in this type of tumor. It seems important to identify patients that may benefit most from the

combination of everolimus and octreotide LAR compared to octreotide LAR alone."

Dr Roberto Labianca from Ospedali Riuniti di Bergamo, Italy, commented: "This large Phase III trial in a rare tumor shows that everolimus is able to increase the efficacy of octreotide LAR, at the present time the standard treatment for advanced neuroendocrine tumors."

"This trial should be considered a practice-changing achievement but it is essential that selection criteria are refined in order to identify the population more likely to respond to this approach," Dr Labianca said. "Further trials in this field are needed, preferably in the frame of a large cooperative collaboration."

Provided by European Society for Medical Oncology