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Anamorelin improve appetite and body mass in patients with cancer anorexia-cachexia

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A new drug, anamorelin, improves appetite and body mass in patients with advanced lung cancer who are suffering cancer anorexia and cachexia, according to phase III data presented at the ESMO 2014 Congress in Madrid, Spain.

"Anorexia and cachexia are among the most troubling and distressing symptoms of advanced cancer, for both patients and their families," says the study's principal investigator, Dr Jennifer Temel from the Department of Medicine, Massachusetts General Hospital, Boston, USA.

Symptoms of the wasting syndrome can include a loss of weight and muscles, together with fatigue, weakness, and loss of appetite. The condition is very common in patients with advanced lung cancer. Anamorelin aims to address the symptoms by mimicking the effects of the so-called "hunger hormone" ghrelin, which is secreted by the stomach.

The large, randomized controlled ROMANA 1 and 2 trials are the first phase III studies examining the impact of anamorelin on anorexia-cachexia in patients with advanced lung cancer.

In the ROMANA studies, patients with unresectable stage III or IV non-small cell lung cancer with cachexia were randomized to receive either 100 mg anamorelin or placebo, given orally each day for 12 weeks.

Among 484 participants in ROMANA 1, those taking anamorelin

experienced a median increase in lean body mass of 1.10 kg in 12 weeks, compared to a loss of 0.44 kg for those taking placebo. Body weight increased in the anamorelin arm by an average of 2.2 kg, compared to 0.14 kg in the placebo arm of the study. Patient symptoms or concerns regarding anorexia-cachexia, including appetite, also significantly improved over 12 weeks in patients taking anamorelin. The most frequent drug-related adverse events included hyperglycemia and nausea.

In ROMANA 2, 495 participants with advanced non-small cell lung cancer experienced similar benefits. Body weight increased by 0.95 kg on average, compared to a loss of 0.57 kg for those receiving placebo, and patient symptoms/concerns regarding anorexia-cachexia significantly improved over 12 weeks.

Patients receiving anamorelin did not experience improvements in their muscle strength, as measured by hand grip strength, although Temel notes that particular test can be difficult to administer in this patient population.

In summary, she says: "Having a safe and well tolerated drug in our armamentarium to improve the incredibly troubling symptoms of anorexia and cachexia will have a dramatic impact on both patients and their families."

Commenting on the results, Associate Professor Florian Strasser from Cantonal Hospital St.Gallen, Switzerland, Chair of the ESMO Palliative Care Working Group, said the results of the Romana trials are promising. "These studies are paving the way towards a multi-component and most likely also a multi-modal treatment for patients suffering from Cancer Anorexia-Cachexia Syndrome."

Cancer anorexia-cachexia syndrome is characterized by four interacting components: loss of muscle mass, decreased nutritional intake, metabolic

and inflammatory alterations driven by active cancer disease, and decreased physical and psychosocial function, Strasser explained. Patients and their family members experience symptoms and concerns associated with each domain such as weakness, loss of appetite, early satiety, taste problems, fatigue or eating-related distress.

"Current management includes nutritional counseling, resistance training and increase of physical activity, psychosocial support and multimodal symptom control. However, these interventions are limited in their effect, and no pharmacological treatment is available to address the relevant components of the syndrome. In addition to quality of life of patients and family members, it has an impact on anticancer treatment efficacy and toxicity as well as survival."

"Both the Romana I and II trials report an improvement of both muscle mass and patients' symptoms and concerns while minimal and manageable side effects occur," Strasser said.

"This is the first anti-cachexia drug for which reports from two placebo-controlled, double blind phase III trials show a consistent effect on different components of the cancer anorexia-cachexia syndrome," Strasser said. "Further data are needed to show whether the increase of muscle mass is accompanied by a gain of fat mass, which would confirm that patients can build reserves while having more appetite. This would be a novel finding: a drug stimulating appetite resulting in more muscle mass and increasing reserves."

Strasser noted that the lack of effect of the drug on hand-grip strength (HGS) as reported in the trial requires further explanation. "HGS measures only upper but not lower extremity strength, and it does not inform enough about physical function and daily living. The populations studied are relatively young and in a good performance status, without information on multimodal management, namely reversible secondary

nutrition impact symptoms. Further data need therefore to show whether the improved symptoms and concerns are related to the known mechanism of the oral ghrelin agonist."

Since both effective anticancer treatment as well as state-of-the-art early integrated palliative medicine with multimodal interventions can improve the cancer anorexia-cachexia syndrome and modify the effects of anti-cachexia drugs, such information is needed to better understand the results, he said.

"Do these trials already show a true clinical benefit, the clinical effectiveness, in a real world population? Probably not yet. The data are promising since the outcomes reported cover more than one relevant component of the CACS and are related to each other. Anamorelin responds to a yet unmet frequent clinical need having an impact on both the patient and the tumour control outcomes with minimal risk," Strasser said.

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