New drug shows improved progression-free survival for patients with advanced metastatic midgut neuroendocrine tumors

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A new therapy in development for the treatment of midgut neuroendocrine tumors, a rare type of cancer that occurs in the small intestine and colon, shows improved progression-free survival and response rates for patients with advanced disease. Results of the international phase 3 clinical trial of lutetium-177 (177Lu)-Dotatate compared to high-dose octreotide LAR were published in the Jan. 12 issue of the *New England Journal of Medicine*.

"Patients diagnosed with midgut neuroendocrine tumors often have advanced disease that has spread to other sites. Treatment options are limited. 177Lu-Dotatate is an effective option to delay tumor progression for patients with this disease," says Jonathan R. Strosberg, head of the Neuroendocrine Tumor Program at Moffitt Cancer Center. "There is also preliminary evidence of survival benefit that requires confirmation on final survival analysis, expected in several years."

Standard treatment for midgut neuroendocrine tumors is hormonal therapy using a somatostatin analog that blocks the growth of tumor cells and reduces the production of hormones that cause symptoms such as flushing and diarrhea. If a patient's tumors progress on somatostatin analog therapy, there are currently not many other treatment options.

Moffitt is one of 41 cancer centers worldwide to investigate a novel therapy, 177Lu-Dotatate. The drug consists of a radioactive molecule

attached to a somatostatin analog, allowing for radiation to be directly targeted to somatostatin receptor expressing tumors. Patients with metastatic or locally advanced midgut neuroendocrine tumors that had disease progression during prior treatment with octreotide, a somatostatin analog, were enrolled in the trial.

Trial results showed that patients who were treated with 177Lu-Dotatate and octreotide had better outcomes than patients who were treated with high-dose octreotide alone. The 20-month progression-free survival rate was 65.2 percent in the 177Lu-Dotatate group and 10.8 percent in the control group. 177Lu-Dotatate-treated patients had a 79 percent lower risk of disease progression or death than the control patients over the follow-up period. Additionally, more patients treated with 177Lu-Dotatate achieved a radiographic response than patients in the control group (18 percent versus 3 percent).

"This is notable given that response rates above 5 percent have not been observed in large randomized clinical trials of other systemic therapies in this patient population," said Dr. Strosberg. "The clinically meaningful and statistically significant improvement in progression-free survival and response rates achieved with treatment of 177Lu-Dotatate when compared to high dose octreotide supports its use in the treatment of neuroendocrine tumor patients. As a clinician treating many patients with this condition, these results bring hope for our ability to improve lives."

The trial data showed that 177Lu-Dotatate-treated patients experienced more adverse events than control patients (86 percent versus 31 percent), but the toxicities were manageable and reversible. The most common adverse events with 177Lu-Dotatate were nausea and vomiting, but this was attributed to amino acid infusions that were given to the patients to relieve potential kidney toxicity. Toxicities that occurred more in the 177Lu-Dotatate-treated patients included thrombocytopenia, anemia,

lymphopenia, and leukopenia.

More information: Jonathan Strosberg et al, Phase 3 Trial ofLu-Dotatate for Midgut Neuroendocrine Tumors, *New England Journal of Medicine* (2017). DOI: 10.1056/NEJMoa1607427