When and How to Use Somatostatin Analogues

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KEYWORDS

• Somatostatin • Receptor • Octreotide • Lanreotide • Pasireotide • Neuroendocrine

KEY POINTS

- Somatostatin analogues are the first-line treatment for control of hormonal excess by hormone-producing neuroendocrine tumors of the gastrointestinal tract and pancreas.
- Somatostatin analogues are the first-line treatment for tumor control of neuroendocrine tumors of the gastrointestinal tract and pancreas.
- To be effective, somatostatin analogues need somatostatin receptor expression on the gastroenteropancreatic neuroendocrine tumor cells.

The research group of the winner of the 1977 Nobel Prize in Physiology or Medicine, Roger Guillemin, discovered the peptide hormone somatostatin.[1] Somatostatin exerts an inhibitory role in the hormone secretion by the pituitary, pancreas, and gastrointestinal tract. It acts via interaction with specific somatostatin receptor (SSTR) subtypes expressed on target tissues. Five human SSTR subtypes have been recognized (named SSTR1–5), each being involved a distinct signaling pathway.[2] SSTR2 predominates in gastrointestinal and pancreatic neuroendocrine tumors (GEP-NETs).[3]

Octreotide was the first biologically stable somatostatin analogue (SSA) that became available.[4] This compound binds with high, low, and moderate affinity to SSTR2, SSTR3, and SSTR5, respectively.[5] A short-acting immediate-release formulation of octreotide (Sandostatin, Novartis, Basel, Switzerland) was initially developed. A long-acting repeatable depot formulation, Sandostatin LAR (Novartis), is currently indicated for long-term treatment of the severe diarrhea and flushing episodes associated with the carcinoid syndrome and long-term treatment of the profuse watery diarrhea associated with VIPomas, as well as for the improvement of progression-free survival (PFS) in patients with unresectable, well-differentiated or moderately differentiated, locally advanced or metastatic NETs from a midgut origin.[6]

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Lanreotide is another SSA that has demonstrated a similar binding profile to the SSTRs to that of octreotide.[5,6] Two different formulations, Lanreotide SR (Ipsen, Boulogne-Billancourt, France) and a long-acting depot formulation, Somatuline Autogel (Ipsen Biopharmaceuticals) are currently available. Somatuline Autogel is, like octreotide, currently indicated for the treatment of the carcinoid syndrome and for the improvement of PFS in patients with unresectable, well-differentiated or moderately differentiated, locally advanced or metastatic GEP-NETs (**Fig. 1**).[6]

INDICATION 1: HORMONAL HYPERSECRETION

SSAs are currently the first-line therapy to control hormone excess and their related syndromes in patients with GEP-NETs. Pooled data from studies using different octreotide and lanreotide formulations in gastrointestinal NET (carcinoid) patients indicate that up to 67% to 74% of patients experience symptomatic relief with SSA treatment.[7–11] Proven efficacy of SSAs for symptom control was also demonstrated in pancreatic NETS, like insulinomas, glucagonomas, VIPomas, and ectopic adrenocorticotrophic hormone, growth hormone receptor hormone, and parathyroid hormone-related peptide-secreting tumors.[12–16] In insulinomas, it is important to closely monitor the blood glucose levels after a therapeutic challenge with a short-acting SSA (octreotide), because, in the potential absence of the expression of specific SSTRs on these tumors, a paradoxic decrease in blood glucose levels can be observed.[17] The latter is

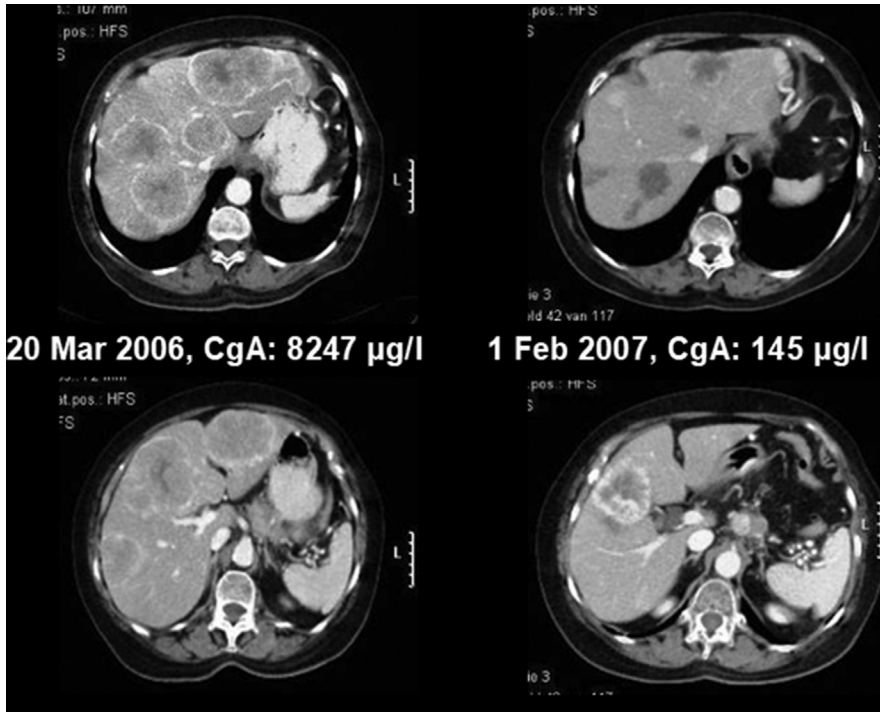

Fig. 1. Computed tomography scan of the abdomen showing extensive liver metastases from a neuroendocrine tumor. Impressive tumor response after the administration of a long-acting somatostatin analogue paralleled by a decrease in circulating chromogranin A (CgA) levels.