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Systemic therapy for unresectable advanced or metastatic pancreatic and midgut neuroendocrine tumours

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Systemic therapy for unresectable advanced or metastatic pancreatic and midgut neuroendocrine tumours

Recommendations

This is a quick reference guide and provides the guideline recommendations only.
For key evidence associated with each recommendation, the systematic review, and the guideline development process, see the Full Report.

GUIDELINE OBJECTIVES

To make recommendations with respect to systemic therapy for the treatment of patients with pancreatic neuroendocrine tumours (pNETs) and midgut neuroendocrine tumours (midgut NETs).

TARGET POPULATION

Adults with a diagnosis of advanced and metastatic pNETs and midgut NETs that have been deemed unresectable after assessment by a neuroendocrine specialist in a multidisciplinary setting.

Patients with neuroendocrine carcinomas (NECs) (i.e., poorly differentiated), malignant neuroblastoma, pituitary tumours, thymic tumours, goblet cell carcinoma, bronchial NETs, paragangliomas, mixed NETs, pheochromocytoma, small cell lung cancer, and thyroid cancer are excluded.

INTENDED USERS

All clinicians involved in the treatment of patients with pNETs and midgut NETs.

PREAMBLE

All patients with gastroenteropancreatic (GEP) NETs should be assessed in a multidisciplinary setting where surgery, whether curative or for optimal debulking, as well as other local therapies are evaluated as treatment options by clinicians with experience in NET care. Individuals should be re-evaluated for resection or local ablative treatment at regular intervals during treatment with systemic therapies.

Of particular relevance to this guideline are the differences in biology, prognosis, and response to therapy between well-differentiated midgut NETs and pNETs. pNETs are more aggressive clinically, with shorter median survival times. Additionally, response rates to systemic therapy are generally higher in pNETs compared to midgut NETs. These differences are reflected in inclusion criteria for many studies in GEP NETs, and subsequently led the Working Group to develop separate recommendations for pNETs and midgut NETs reflected in this document. Recommendations 2 and 3 discuss systemic therapy options in patients with unresectable advanced or metastatic pNETs and midgut NETs, respectively. The sequencing of the various classes of treatments have not been compared head-to-head. As a result, there is insufficient evidence for recommendations on sequencing of therapy; however, the Working Group has provided some guidance, where possible, based on the inclusion criteria used in specific trials and expert opinion in the qualifying statements.

RECOMMENDATIONS

Recommendation 1
Unresectability and inoperability should be established after assessment in a multidisciplinary setting where treatment options, such as surgery or other local therapies, are considered by experienced care providers.

Recommendation 2
For patients with unresectable advanced or metastatic pNETs:

2.1 Somatostatin analogues
Patients with Ki-67 <10% and somatostatin receptor 2 (SSTR2)-positivity should be offered lanreotide. Based on expert opinion, the use of sustained-release octreotide is also acceptable. Pasireotide is not indicated for use in these patients.

2.2 Chemotherapy
Patients with grade 1 or 2 tumours can be offered chemotherapy with capecitabine plus temozolomide upon progression from somatostatin analogues (SSAs) or as first-line therapy in clinical scenarios with more aggressive disease where clinical response is required.

2.3 Targeted therapy
Patients with grade 1 or 2 tumours can be offered sunitinib or everolimus.

2.4 Peptide Receptor Radionuclide Therapy
Patients with SSTR-positive tumours may be offered peptide receptor radionuclide therapy (PRRT).

2.5 Immunotherapy
The use of immunotherapy is not recommended outside of a clinical trial.

Recommendation 3
For patients with unresectable advanced or metastatic midgut NETs:

3.1 SSAs
Patients with Ki-67 <10% should be offered lanreotide or sustained-release octreotide.

3.2 PRRT
The use of PRRT with ^{177}Lu-DOTATATE in combination with SSA treatment is recommended in patients with SSTR2-positive, grade 1 to 2 NETs after progression on an SSA.

3.3 Targeted therapy
Patients with non-functional grade 1 or 2 tumours may be offered everolimus.

3.4 Chemotherapy
There is insufficient evidence for or against the use of chemotherapy.

3.5 Immunotherapy
The use of immunotherapy is not recommended outside of a clinical trial.