

NCCN Guidelines for Neuroendocrine and Adrenal Tumors V.1.2020 – Annual 11/18/19

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
<p>General External request:</p> <p>Submission from Genentech to consider including entrectinib and appropriate NTRK gene fusion testing for the treatment of NTRK gene fusion-positive neuroendocrine cancers.</p>	<p>Based on a review of data and discussion, the panel consensus did not support the inclusion of entrectinib and appropriate NTRK gene fusion testing for the treatment of NTRK gene fusion-positive neuroendocrine cancer, based on limited available data.</p>	0	24	0	4
<p>NET-1 External request:</p> <p>Submission from Curium to include copper Cu 64 dotatate as an option where somatostatin receptor-based imaging is recommended throughout the guideline.</p>	<p>The panel consensus was to defer the submission until FDA approval.</p>	0	24	0	4
<p>NET-7 Internal request:</p> <p>Comment to reassess inclusion of chemoradiation as an adjuvant therapy option for intermediate grade (atypical) bronchopulmonary NET.</p>	<p>Based on the discussion, the panel consensus was to remove chemoradiation as an adjuvant therapy option for intermediate grade (atypical) bronchopulmonary NET due to limited available data.</p>	0	15	7	6
<p>NET-8 Internal request:</p> <p>Comment to reassess the inclusion of platinum/etoposide as a primary therapy option for low grade (typical), locoregional unresectable bronchopulmonary/thymus NET.</p>	<p>Based on the discussion, the panel consensus was to remove cisplatin/etoposide and carboplatin/etoposide from the primary therapy option for low grade (typical), locoregional unresectable bronchopulmonary/thymus NET.</p>	0	24	0	4
<p>NET-8 Internal request:</p> <p>Comment to consider the inclusion of the following primary therapy options for intermediate grade (atypical), locoregional unresectable bronchopulmonary/thymus NET:</p> <ul style="list-style-type: none"> • Everolimus • Octreotide or lanreotide 	<p>Based on the discussion, the panel consensus was to include everolimus as a primary therapy option for intermediate grade (atypical), locoregional unresectable bronchopulmonary/thymus NET. This is a category 2A recommendation.</p> <p>Based on the discussion, the panel consensus was to include octreotide or lanreotide as a primary therapy option for intermediate grade (atypical), locoregional unresectable bronchopulmonary/thymus NET, if somatostatin receptor positive and/or hormonal symptoms. This is a category 2A recommendation.</p>	24	0	0	4
		24	0	0	4

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<p>NET-8/NET-10/NET-11/AGT-5 External Request:</p> <p>Submission from the Society of Interventional Radiology to consider:</p> <ol style="list-style-type: none"> Including a section on Principles of Liver-Directed Therapy (LDT). Add ablation as a potential alternative treatment option for unresectable primary typical (low grade) bronchopulmonary/thymus NET. (NET-8) Add LDT as an option for metastatic bronchopulmonary/thymus NET with liver dominant liver metastases. (NET-10) Change “hepatic-directed therapy” to “liver-directed therapy”. (NET-11 & PanNET-7) Under treatment for metastatic adrenal tumors, consider changing local therapy with RFA to ablative therapies, and consider LDT for liver metastases. (AGT-5) 	<p>1. Based on a review of data and discussion, the panel consensus supported the inclusion of a section on “Principles of Liver-Directed Therapy for Neuroendocrine Tumor Metastases.”</p>	24	0	0	4
	<p>2. Based on a review of data and discussion, the panel did not add ablation as a potential alternative treatment option for unresectable primary typical (low grade) bronchopulmonary/thymus NET. However, the panel supported adding the following language to footnote cc: For symptom control, consider addition of focal therapy (ie, endobronchial therapy).</p>	0	24	0	4
	<p>3. Based on the discussion, the panel consensus supported the inclusion of LDT as an option for liver-predominant metastatic bronchopulmonary/thymus NET, for patients with clinically significant tumor burden and low grade (typical) disease, or evidence of disease progression, or intermediate grade (atypical) disease, or symptomatic disease.</p>	24	0	0	4
	<p>4. Based on the discussion, the consensus supported changing “hepatic-directed therapy” to “liver-directed therapy” and a footnote was added to the Principles of Liver-Directed Therapy for Neuroendocrine Tumor Metastases. (NET-11 and PanNET-7)</p>	24	0	0	4
	<p>5. Based on the discussion, the consensus supported changing the “RFA” local therapy option to “thermal ablative therapy” and a link was added to the Principles of Liver-Directed Therapy for Neuroendocrine Tumor Metastases.</p>	24	0	0	4

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<p>NET-10 Internal request:</p> <p>Comment to reassess the evidence for everolimus for the treatment of metastatic bronchopulmonary NET.</p>	<p>Based on the discussion and noted reference, the panel consensus was that everolimus is supported by high-level evidence and the category was changed from a category 2A to a category 1 recommendation for metastatic bronchopulmonary NET, for patients with clinically significant tumor burden and low grade (typical) disease, or evidence of disease progression, or intermediate grade (atypical) disease, or symptomatic disease.</p> <p>Reference: Fazio N, Buzzoni R, Delle Fave G, et al. Everolimus in advanced, progressive, well-differentiated, non-functional neuroendocrine tumors: RADIANT-4 lung subgroup analysis. Cancer Sci. 2018;109(1):174-181.</p>	24	0	0	4
<p>NET-12 External request:</p> <p>Submission from Lexicon Pharmaceuticals to consider including telotristat ethyl as a first choice along with SSAs to treat carcinoid syndrome diarrhea inadequately controlled by SSA therapy rather than increasing dose and/or frequency of SSAs.</p>	<p>Based on a review of data and discussion, the panel consensus was to not make changes to the current recommendations.</p>	0	24	0	4
<p>PanNET-3 Internal request:</p> <p>Comment to consider adding everolimus as an option for stabilizing glucose levels in locoregional disease.</p>	<p>Based on the discussion, the panel consensus was to include everolimus as an option for stabilizing glucose levels in patients with locoregional disease. This can be used alone, or in combination with diet and/or diazoxide. This is a category 2A recommendation.</p>	24	0	0	4
<p>AGT-5 External request:</p> <p>Submission from EMD Serono, Inc., to consider adding avelumab as an option for metastatic adrenal gland tumors.</p>	<p>Based on a review of data and discussion, the panel consensus did not support the inclusion of avelumab as an option for metastatic adrenal gland tumors due to insufficient available data.</p>	1	16	4	7

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<p>AGT-5 Internal request:</p> <p>Comment to consider inclusion of pembrolizumab as an option for unresectable/metastatic adrenocortical tumors.</p>	<p>Based on the data in the noted references and discussion, the panel consensus was to include pembrolizumab +/- mitotane as an option for metastatic adrenal gland tumors. This is a category 2A, other recommended regimen.</p> <p>References:</p> <ul style="list-style-type: none"> Raj NP, Zheng Y, Kelly V, et al. Efficacy and safety of pembrolizumab in patients with advanced adrenocortical carcinoma. Journal of Clinical Oncology 2019;37(15_suppl), 4112-4112. Marabelle et al. Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair-deficient cancer: results from the phase 2 KEYNOTE-158 study. J Clin Oncol 38:1-10. 	12	2	8	6
<p>NE-E (3 of 4) Internal request:</p> <p>Comment to consider inclusion of the following cytotoxic chemotherapy options for locoregional advanced/metastatic pancreatic NET:</p> <ul style="list-style-type: none"> FOLFOX (leucovorin + 5-FU + oxaliplatin) CAPEOX (capecitabine + oxaliplatin) 	<p>Based on the data in the noted reference and discussion, the panel consensus was to include FOLFOX as an option for locoregional advanced/metastatic pancreatic NET, for those with bulky, symptomatic, and/or progressive disease. This is a category 2A, other recommended regimen.</p>	24	0	0	4
	<p>Based on the data in the noted reference and discussion, the panel consensus was to include CAPEOX as an option for locoregional advanced/metastatic pancreatic NET for those with bulky, symptomatic, and/or progressive disease. This is a category 2A, other recommended regimen.</p> <p>References:</p> <ul style="list-style-type: none"> Kunz PL, Balise RR, Fehrenbacher L, et al. Oxaliplatin-fluoropyrimidine chemotherapy plus bevacizumab in advanced neuroendocrine tumors: an analysis of 2 phase II trials. Pancreas. 2016;45(10):1394-1400. Spada F, Antonuzzo L, Marconcini R, et al. Oxaliplatin-based chemotherapy in advanced neuroendocrine tumors: clinical outcomes and preliminary correlation with biological factors. Neuroendocrinology. 2016;103(6):806-814. 	24	0	0	4