Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
WDG3-1/AGT-5/NET-9/NET-10/PanNET-7/PHEO-2/NE-D External request: Submission from Foundation Medicine, Inc. on (9/18/2020) Consider the following changes: • Amending the algorithm on pages to recommend tumor mutational burden (TMB) as determined by a validated and/or FDA-approved assay to inform the use of pembrolizumab. • Add a footnote referencing Merino DM, et al. J Immunother Cancer 2020;8:e000147. • Add pembrolizumab as a treatment option for patients with unresectable or metastatic tumors with tissue tumor mutational burden-high (tTMB-H) ≥10 mutations/megabase, as determined by an FDA-approved test, who have progressed following prior treatment and who have no satisfactory alternative treatment options. (NE-D-1 through 4)	Based on a review of the data and discussion, the panel consensus supported the inclusion of TMB testing per FDA approved test for the following: • Well-differentiated grade 3 neuroendocrine tumors (NET) (WDG3-1) • Poorly differentiated neuroendocrine carcinoma (see footnote d on PDNEC-1) • Adrenocortical carcinoma (AGT-5),	26	0	0	5
	Based on a review of the data and discussion, the panel consensus did not support the inclusion of TMB testing for GI or bronchopulmonary/thymus NET (NET-9/10), Pancreatic NET (PanNET-7), or pheochromocytoma (PHEO-2/3)	0	26	0	5
	Based on a review of the data and discussion, the panel consensus supported the inclusion of pembrolizumab as an option for well-differentiated grade 3, locally advanced/metastatic neuroendocrine tumors with unfavorable biology, if TMB-H (≥10 muts/Mb), that have progressed following prior treatment and have no satisfactory alternative treatment options. This is a category 2A recommendation.	26	0	0	5
	The panel consensus was to revise the footnotes on PDNEC-1 and AGT-5 to clarify that an FDA approved test is recommended for determination of TMB.	26	0	0	5
	The panel consensus did not support the inclusion of pembrolizumab for the following indications: • Locoregional advanced and/or metastatic NET of the GI tract (well-differentiated grade 1/2) (NE-F 1 of 5) • Metastatic bronchopulmonary/thymus NET (NE-F 2 of 5) • Locoregional advanced and/or metastatic pancreatic NET (NE-F 3 of 5) See Submission for references,	0	26	0	5

WDG3-1
Internal request:
 	
Comment to consider the addition of treatment recommendations for well-differentiated grade 3 neuroendocrine tumors.
	Based on a review of the data and discussion, the panel consensus was to include treatment recommendations for well-differentiated grade 3 NET:
	Locoregional (resectable) disease: Neoadjuvant systemic therapy options
	• Temozolomide +/- capecitabine
	• Oxaliplatin-based therapy (FOLFOX, CAPEOX)
	• Cisplatin/etoposide or carboplatin/etoposide
	Unresectable locally advanced/metastatic disease with favorable biology: Systemic therapy options
	• Asymptomatic/low tumor burden:
	   o Octreotide or lanreotide (if SSR-positive and/or hormonal symptoms)
	• Clinically significant tumor burden or evidence of disease progression:
	   o Octreotide or lanreotide (if SSR-positive and/or hormonal symptoms)
	   o PRRT with 177Lu-DOTATATE
	   o Everolimus
	   o Sunitinib (pancreas only)
	   o Pembrolizumab for TMB-H tumors (≥10 muts/Mb) (category 2B; see transparency dated 03/26/21 for vote)
	   o Chemotherapy (ie, temozolomide +/- capecitabine, FOLFOX, CAPEOX, cisplatin/etoposide, or carboplatin/etoposide)
	Locally advanced/metastatic disease with unfavorable biology: Systemic therapy options
	• Cisplatin/etoposide
	• Carboplatin/etoposide
	• Temozolomide +/- capecitabine
	• Oxaliplatin-based therapy (ie, FOLFOX or CAPEOX)
	• Pembrolizumab for TMB-H tumors (≥10 muts/Mb)
	• Irinotecan-based therapy (eg. FOLFIRI, cisplatin + irinotecan, or FOLFIRINOX) (see transparency dated 03/26/21 for vote)
	• Nivolumab + ipilimumab (category 2B; see transparency dated 03/26/21 for vote)
		26	0	0	5