

Evidence Discussion (ONC 31.8)

Extrathoracic Small Cell and Large Cell Neuroendocrine Tumors

Poorly differentiated/high grade neuroendocrine tumors (NET) may occur anywhere in the body and exhibit more aggressive behavior than other neuroendocrine tumors. When these tumors occur in the lung, they are managed like small cell lung cancer and the small-cell lung cancer guidelines apply. This section refers to extrathoracic, poorly-differentiated or high-grade NETs.

Initial Staging

EviCore guidelines align with NCCN guidelines, and supports initial staging with contrasted CT of the chest, abdomen and pelvis, with sensitivity and specificity ranging from 82-100% (Półtorak-Szymczak 2021, Bergsland 2023). Metastatic disease, particularly to the liver, is common with this entity with in this setting (Walter 2017, NCI 2024). MRI is supported if CT is unclear for liver involvement as noted in eviCore guideline ONC 31.2. Given the undifferentiated nature of these tumors, dotatate PET/CT is not routinely supported as they do not consistently have somatostatin receptors, with some studies showing this modality missing 50% of tumors (NCI 2024). Sensitivity and specificity of FDG PET/CT is superior to somatostatin-receptor based imaging for undifferentiated tumors, but is still widely variable and is not supported for first line imaging but may be used as a problem solving tool when conventional imaging is inconclusive (Bergsland 2023, Kaewput 2022). Poorly differentiated NETs do have a propensity for CNS involvement, and MRI brain with and without contrast is supported for initial staging with head and neck primary site or for any signs and symptoms suggestive of CNS involvement (Bergsland 2023, NCI 2024). Suspected bony metastatic disease may be evaluated using eviCore guideline ONC 31.5.

Restaging and suspected recurrence

In alignment with NCCN,conventional imaging with contrasted CT of the chest, abdomen, pelvis and any other involved sites may be repeated every 2 cycles of treatment. In the case of suspected recurrence, CT chest, abdomen and pelvis with contrast are supported as well and MRI brain and bone scan, in alignment with NCCN (Bergsland 2023). FDG PET/CT is not routinely supported in this setting for the reasons cited in the section on initial staging, but eviCore recognizes the potential of PET/CT as a problem-solving tool in this setting and allows for medical director flexibility in rare circumstances in the interest of patient safety.

Surveillance

EviCore Guidelines for surveillance align with the NCCN, and support CT chest, abomden and pelvis every 3 months for the first year, then every 6 months for 4 additional years, then annually indefinitely due to the long term risk of recurrence in this entity (Walter 2023, NCI 2024, Bergsland 2023). While the NCCN supports CT or MRI for the abdomen and pelvis, CT has excellent sensitivity and specificity in this setting and is the preferred first-line surveillance imaging by eviCore guidelines (Półtorak-Szymczak 2021, Kaewput 2022).

References

1. Bergsland E, Halfdanarson T, Lieu C et al. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroendocrine and Adrenal Tumors Version 1.2023-August 2, 2023. All rights reserved. Accessed [June 14, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org
2. Walter T, Tougeron D, Baudin E, Le Malicot K, Lecomte T, Malka D, Hentic O, Manfredi S, Bonnet I, Guimbaud R, Coriat R, Lepère C, Desauw C, Thiot-Bidault A, Dahan L, Roquin G, Aparicio T, Legoux JL, Lombard-Bohas C, Scoazec JY, Lepage C, Cadiot G; CEPD investigators. Poorly differentiated gastro-entero-pancreatic neuroendocrine carcinomas: Are they really heterogeneous? Insights from the FFCD-GTE national cohort. *Eur J Cancer*. 2017 Jul;79:158-165. doi: 10.1016/j.ejca.2017.04.009. Epub 2017 May 11. PMID: 28501762.
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