

Evidence Discussion (ONC 30.3)

Paraneoplastic Syndromes

Cross sectional imaging with contrasted CT of the chest, abdomen and pelvis is generally considered first-line to look for visceral malignancy in most paraneoplastic syndromes. While sensitivity varies widely (30-82% across studies), specificity is reasonable (71-100%) (Sheikhabahaei 2017). PET/CT is supported in patients with documented paraneoplastic antibodies, inconclusive conventional imaging, or to assess for alternate biopsy sites when an abnormality is found on conventional imaging that is inaccessible for biopsy. The sensitivity and specificity of PET/CT is approximately 80%, when used to evaluate patients who had negative or unclear conventional imaging (Harlos 2019). PET/CT is not supported as first line imaging as PET may miss smaller tumors, and has a false negative rate of approximately 20% in this setting (Sheikhabahaei 2017). While there is a lack of prospective data on monitoring paraneoplastic syndromes, it is known that these phenomena may precede detectable malignancy. In the interest of patient safety, eviCore GL support repeat CT imaging every 6 months for 4 years; for Lambert-Eaton Syndrome, 2 years is sufficient as 96% of associated SCLC is detected in the first year, with later reports generally from an era of lesser quality CTs. (Pelosof 2010, Badawy 2023, Titulauer 2011).

Venous thromboembolism in the absence of a hypercoagulable risk factor may suggest occult malignancy. Blood testing, exam and non-advanced imaging have been shown to be helpful in most cancers that present with a first unprovoked DVT, but other advanced imaging is not cost-effective without other symptoms suggesting malignancy in this setting. In the setting of a second unprovoked DVT, cross sectional imaging with contrasted CT may be considered and is supported by eviCore guidelines (Badawy 2023, Harachi 1998, Rutherford 2007, Schwartzbach 2012).

Systemic mastocytosis may also develop extramedullary involvement and end-organ dysfunction, particularly involving liver and spleen. CT or MRI of abdomen and pelvis are supported in alignment with the NCCN. There is no NCCN recommendation for PET/CT in systemic mastocytosis.

References

1. Harlos C, Metser U, Poon R, MacCrostie P, Mason W. **18 F-Fluorodeoxyglucose positron-emission tomography for the investigation of malignancy in patients with suspected paraneoplastic neurologic syndromes and negative or indeterminate conventional imaging: a retrospective analysis of the Ontario PET Access Program, with systematic review and meta-analysis.** *Curr Oncol.* 2019 Aug;26(4):e458-e465. doi: 10.3747/co.26.4583. Epub 2019 Aug 1. PMID: 31548813; PMCID: PMC6726279.
2. Pelosof LC, Gerber DE. Paraneoplastic syndromes: an approach to diagnosis and treatment. *Mayo Clin Proc.* 2010 Sep;85(9):838-54. doi: 10.4065/mcp.2010.0099. Erratum in: *Mayo Clin Proc.* 2011 Apr;86(4):364. Dosage error in article text. PMID: 20810794; PMCID: PMC2931619.
3. Badawy M, Revzin MV, Consul N, Soliman M, Ganeshan DM, Heymann JC, Gaballah AH, Rao Korivi B, Morani AC, Javadi S, Elsayes KM. Paraneoplastic Syndromes from Head to Toe:

Pathophysiology, Imaging Features, and Workup. *Radiographics*. 2023 Mar;43(3):e220085. doi: 10.1148/rg.220085. PMID: 36795597.

4. Sundermann B, Schröder JB, Warnecke T, et al. Imaging Workup of Suspected Classical Paraneoplastic Neurological Syndromes: A Systematic Review and Retrospective Analysis of 18F-FDG-PET-CT. **Acad Radiol** 2017;24(10):1195–1202.
5. Sheikhabaei S, Marcus CV, Fragomeni RS, Rowe SP, Javadi MS, Solnes LB. Whole-Body 18F-FDG PET and 18F-FDG PET/CT in Patients with Suspected Paraneoplastic Syndrome: A Systematic Review and Meta-Analysis of Diagnostic Accuracy. **J Nucl Med** 2017;58(7):1031–1036.
6. Titulaer MJ, Soffieti R, Dalmau J, et al. Screening of tumours in paraneoplastic syndromes: report of an EFNS task force. *Eur J Neurol*. 2011;18(1):19–e3. doi:10.1111/j.1468-1331.2010.03220.x.
7. Harachchi RJK, Lok J, Prins MH, Büller HR, Prandoni P. Undiagnosed malignancy in patients with deep vein thrombosis: incidence, risk indicators, and diagnosis. *Cancer* 1998;83(1):180–185.
8. Rutherford GC, Dineen RA, O'Connor A. Imaging in the investigation of paraneoplastic syndromes. *Clin Radiol* 2007;62(11):1021–1035
9. Schwarzbach CJ, Schaefer A, Ebert A, et. al. Stroke and cancer: the importance of cancer-associated hypercoagulation as a possible stroke etiology. *Stroke*. 2012;43(11):3029-3034. doi:10.1161/STROKEAHA.112.658625.
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10. Gerds A, Jain T, Oh s. National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2024 – April 24, 2024. Systemic Mastocytosis. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) ©2024 National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.