

Evidence Discussion (ONC 27.1-27.2)

Suspected lymphoma and DLBCL

Initial Staging

- Evicore guidelines for initial staging align with NCCN and support either PET/CT or diagnostic CTs. Greater than 97 percent of DLBCL are FDG-avid, though it is not known to be more accurate than CT for DLBCL at initial staging. However, baseline PET may be useful for comparison, as end of treatment remission assessment with PET-CT is more accurate than CT alone in DLBCL (Barrington 2014).

Restaging

- CT is supported every 2 cycles, but PET/CT is generally not supported for interim restaging until after 3-4 cycles of therapy and at the end of chemotherapy and/or radiation, due to a high rate of false positive results (ranging from 11-90%) for restaging during treatment (Tokola 2021, Zelenetz 2024). PET-CT remains standard for remission assessment at end of therapy, where it's accuracy is greater than CT alone for DLBCL (Barrington 2014, Zelenetz 2024). Documentation of residual tissue at end of therapy is useful for monitoring for relapse, and as such diagnostic, contrast enhanced CT is supported if requested in addition to PET at end of therapy (Barrington 2014, Zelenetz 2024).
- FDG avidity is prognostic for relapsed/refractory DLBCL and may have a role in patient selection for CAR-T therapy and to assess response, so is supported as a baseline before CAR-T and once 30-60 days after completion, to assess response and identify patients who may be candidates for further salvage therapy (Barrington 2014, Zelenetz 2024)

Surveillance

- The false-positive rate with PET scans for surveillance in various studies is 16-20%, potentially leading to unnecessary investigations, radiation exposure, biopsies, expense, and patient anxiety (Cheson 2014, Lynch 2014, ASCO 2021). Several small studies have failed to note an improvement in relapse detection with CT over clinical observation in DLBCL, however, there is no definitive standard for surveillance imaging with CT (Thompson 2014, ElGalaly 2015). The majority of relapses occur in the first 2 years, and the NCCN supports CT imaging of involved areas and chest, abdomen and pelvis every 6 months for the first two year. In the interest of patient and provider centricity, eviCore guidelines align with the NCCN with respect to surveillance in DLBCL.

References

1. Paquin AR, Oyogoa E, McMurry HS, et al. The diagnosis and management of suspected lymphoma in general practice. *Eur J Haematol*. 2023 January ; 110(1): 3–13. doi:10.1111/ejh.13863

2. Kühnl A, Cunningham D, Hutka M, Peckitt C, Rozati H, Morano F, Chong I, Gillbanks A, Wotherspoon A, Harris M, Murray T, Chau I. Rapid access clinic for unexplained lymphadenopathy and suspected malignancy: prospective analysis of 1000 patients. *BMC Hematol.* 2018 Aug 14;18:19. doi: 10.1186/s12878-018-0109-0. PMID: 30128155; PMCID: PMC6092787.
3. Bosch X, Coloma E, Donate C, Colomo L, Doti P, Jordán A, López-Soto A. Evaluation of unexplained peripheral lymphadenopathy and suspected malignancy using a distinct quick diagnostic delivery model: prospective study of 372 patients. *Medicine (Baltimore).* 2014 Oct;93(16):e95. doi: 10.1097/MD.0000000000000095. PMID: 25310744; PMCID: PMC4616296.
4. Nixon S, Bezverbnaya K, Maganti M, Gullane P, Reedijk M, Kuruvilla J, Prica A, Kridel R, Kukreti V, Bennett S, Rogalla P, Delabie J, Pintilie M, Crump M. Evaluation of Lymphadenopathy and Suspected Lymphoma in a Lymphoma Rapid Diagnosis Clinic. *JCO Oncol Pract.* 2020 Jan;16(1):e29-e36. doi: 10.1200/JOP.19.00202. Epub 2019 Oct 1. PMID: 31573831.
5. Zelenetz A, Gordon L, Abramson J, et al. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas Version 1.2024 — January 18, 2024. All rights reserved. Accessed [March 12, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org.
6. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, Lister TA; Alliance, Australasian Leukaemia and Lymphoma Group; Eastern Cooperative Oncology Group; European Mantle Cell Lymphoma Consortium; Italian Lymphoma Foundation; European Organisation for Research; Treatment of Cancer/Dutch Hemato-Oncology Group; Grupo Español de Médula Ósea; German High-Grade Lymphoma Study Group; German Hodgkin's Study Group; Japanese Lymphoma Study Group; Lymphoma Study Association; NCIC Clinical Trials Group; Nordic Lymphoma Study Group; Southwest Oncology Group; United Kingdom National Cancer Research Institute. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol.* 2014 Sep 20;32(27):3059-68. doi: 10.1200/JCO.2013.54.8800. PMID: 25113753; PMCID: PMC4979083.
7. Barrington SF, Mikhaeel NG, Kostakoglu L, Meignan M, Hutchings M, Müller SP, Schwartz LH, Zucca E, Fisher RI, Trotman J, Hoekstra OS, Hicks RJ, O'Doherty MJ, Hustinx R, Biggi A, Cheson BD. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. *J Clin Oncol.* 2014 Sep 20;32(27):3048-58. doi: 10.1200/JCO.2013.53.5229. Erratum in: *J Clin Oncol.* 2016 Jul 20;34(21):2562. PMID: 25113771; PMCID: PMC5015423.
8. Tokola S, Kuitunen H, Turpeenniemi-Hujanen T, Kuittinen O. Interim and end-of-treatment PET-CT suffers from high false-positive rates in DLBCL: Biopsy is needed prior to treatment decisions. *Cancer Med.* 2021 May;10(9):3035-3044. doi: 10.1002/cam4.3867. Epub 2021 Mar 31. PMID: 33792190; PMCID: PMC8085947.
9. Lynch RC, Zelenetz AD, Armitage JO, Carson KR. Surveillance imaging for lymphoma: pros and cons. *Am Soc Clin Oncol Educ Book.* 2014:e388-95. doi: 10.14694/EdBook_AM.2014.34.e388. PMID: 24857129.
10. ASCO. (2021). Choosing Wisely. Retrieved from <https://old-prod.asco.org/news-initiatives/current-initiatives/cancer-care-initiatives/value-cancer-care/choosing-wisely>

11. **Thompson CA**, Ghesquieres H, Maurer MJ, et al. Utility of routine post-therapy surveillance imaging in diffuse Large B-Cell Lymphoma. *J Clin Oncol.* 2014;32(31):3506-3512. doi:10.1200/JCO.2014.55.7561.
12. El-Galaly TC, Jakobsen LH, Hutchings M, et al. Routine imaging for diffuse Large B-Cell Lymphoma in first complete remission does not improve post-treatment survival: a Danish-Swedish population-based study. *J Clin Oncol.* 2015;33(34):3993-3998. doi:10.1200/JCO.2015.62.0229.