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Practical Approach to Imaging in Patients with Lymphoma

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Disclosures

- No financial disclosures

Objectives

- Identify imaging modalities for Hodgkin Lymphoma and Non-Hodgkin Lyphoma patients
- Identify utility of imaging through continuum of care of lymphoma patients

References

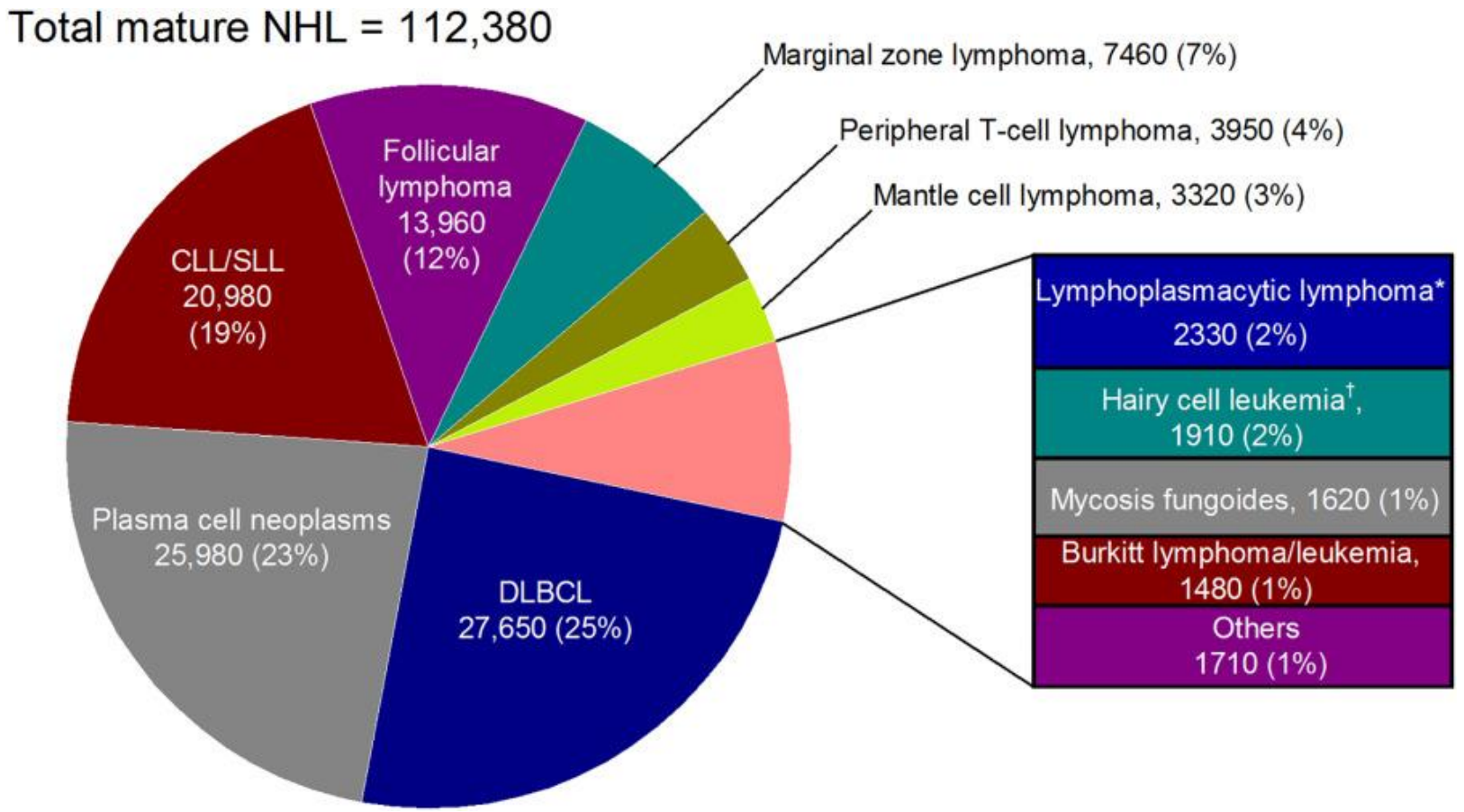
Types of Lymphoma

- Hodgkin Lymphoma
  - Classic Hodgkin Lymphoma
  - Nodular lymphocyte predominant Hodgkin Lymphoma

- Non-Hodgkin Lymphoma
  - Diffuse Large B Cell Lymphoma
  - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
  - Follicular Lymphoma
  - Mantle Cell Lymphoma
  - Marginal Zone Lymphoma
  - Burkitt Lymphoma
  - Lymphoplasmacytic Lymphoma
  - T Cell Lymphoma

References

2016 US lymphoid malignancy statistics by World Health Organization subtypes



CA: A Cancer Journal for Clinicians, Volume: 66, Issue: 6, Pages: 443-459, First published: 12 September 2016, DOI: (10.3322/caac.21357)

References

Types of Imaging Studies

- Computed Tomography (CT)
  - Use X-rays for cross-sectional images of the body
- Positron Emission Tomography (PET)
  - Use of radioactive tracer, fluorodeoxyglucose (FDG), to detect glucose metabolism in the body
- Magnetic Resonance Imaging (MRI)
  - Use of magnetic and radio waves as opposed to x-rays to provide detailed images of soft tissues in the body.
  - Ideal for imaging the spinal cord or brain

References

American College of Radiology: Patient Considerations

CT

- Requires fasting
- Patient specific parameters:
  - Allergies (contrast dye)
  - Renal function
  - Medications (metformin)

PET-CT

- Requires fasting (4 hours)
- 1 Liter of water 2 hours prior to exam
- 24 hours Prior:
  - No vigorous activity
  - Low carb meals
  - No alcohol

MRI

- No metal devices
- Requires fasting
- Patient specific parameters:
  - Allergies (contrast dye)
  - Renal function
  - Medications (metformin)

American College of Radiology. ACR-SPR Practice Parameters for Performing FDG-PET/CT in Oncology. 2016. Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/FDG-PET-CT.pdf?la=en. Accessed August 5, 2020

American College of Radiology. ACR Manual on Contrast Media 2016. Available at: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf. Accessed August 5, 2020

References

ACR Indications for PET-CT in Cancer

- Staging with initial presentation to guide treatment selection
- Monitor response to therapy
- Determine anatomical extent of disease
- Restage in the setting of relapse of disease
- Further characterize abnormality noted on different imaging modality
- Verify presence of disease, specifically with clinical symptoms, tests (i.e. tumor markers)
- Guide radiation therapy or biopsy

American College of Radiology. ACR-SPR Practice Parameters for Performing FDG-PET/CT in Oncology. 2016. Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/FDG-PET-CT.pdf?la=en. Accessed August 5, 2020

References

PET-CT Scoring System

Deauville 5 Point Scale

1. No uptake above the background
2. Uptake ≤ mediastinum
3. Uptake > mediastinum, but ≤ liver
4. Uptake moderately > liver
5. Uptake markedly higher than liver and/or new lesions

X. New areas of uptake unlikely to be related to lymphoma

American College of Radiology. ACR-SPR Practice Parameters for Performing FDG-PET/CT in Oncology. 2016. Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/FDG-PET-CT.pdf?la=en. Accessed August 5, 2020

References

Timeframe and Indication of Imaging Modalities

Staging:

- To determine extent of disease

Monitoring Treatment Response:

- Response Criteria to therapy

Surveillance:

- Identify relapse disease, transformation

Lugano Response Criteria

Response	Site	PET-CT Based Criteria	CT Based Response
Complete	Lymph nodes and extralymphatic sites	Complete metabolic response Deauville Score: 1, 2, 3	Target nodes/nodal masses must regress to ≤1.5 cm in LDi; No extralymphatic sites
	Nonmeasured lesions	Not applicable	Absent
	Organ Enlargement	Not applicable	Regress to normal
	New lesions	None	None
	Bone marrow	No evidence of FDG avid disease	Normal by morphology
Partial	Lymph nodes and extralymphatic sites	Partial metabolic response Deauville: 4 or 5	≥50% decrease in SPD of up to 6 target nodes
	Nonmeasured lesions	Not applicable	Absent/normal, regressed but no increase
	Organ Enlargement	Not applicable	Spleen must regress by >50% in length
	New lesions	None	None
	Bone marrow	Residual uptake higher than uptake in normal marrow but reduced from baseline	Not applicable

Cheson, B., Fisher, R., Barrington, S., Cavalli, F., Schwartz, L., Zucca, E., & Lister, T. (2014). Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. Journal of Clinical Oncology, 32(27), 3059–3067. https://doi.org/10.1200/jco.2013.54.8800

References

Lugano Response Criteria

Response	Site	PET-CT Based Criteria	CT Based Response
No Response Stable Disease	Target nodes/nodal masses, extra nodal masses	No metabolic response; Deauville Score: 4 or 5 with no significant change in FDG uptake from baseline at interim or end of treatment	< 50% decrease from baseline in SPD of up to 6 dominant, measurable nodes and extranodal site. No progressive disease criteria met
	Nonmeasured lesions	Not applicable	No increase consist with progression
	Organ Enlargement	Not applicable	No increase consist with progression
	New lesions	None	None
	Bone marrow	No change from baseline	Not applicable
Progressive Disease	Individual target nodes/nodal masses, extranodal lesions	Deauville Score: 4 or 5 with increase in FDG; new FDG avid foci consistent with lymphoma at interim or end of treatment	Node/lesion: LDi> 1.5 cm and increase by 50%
	Nonmeasured lesions	None	New or clear progression or preexisting nonmeasured lesions
	New lesions	New FDG –avid foci consistent with lymphoma	Regrowth of previously resolved lesions; a new node >1.5 cm or new extranodal site >1.0 cm. Assessable disease of any size attributable only to lymphoma
	Bone marrow	New or recurrent FDG-avid foci	New or recurrent involvement

Cheson, B., Fisher, R., Barrington, S., Cavalli, F., Schwartz, L., Zucca, E., & Lister, T. (2014). Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. Journal of Clinical Oncology, 32(27), 3059–3067. https://doi.org/10.1200/jco.2013.54.8800

Hodgkin Lymphoma

Staging Initial Work Up:

- CT: contrast enhanced for diagnostic purposes

- PET-CT: Skull base to mid thigh
    - If PET-CT is completed, bone marrow biopsy with aspirate is not considered routine evaluation for HL staging

Cheson, B., Fisher, R., Barrington, S., Cavalli, F., Schwartz, L., Zucca, E., & Lister, T. (2014). Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. Journal of Clinical Oncology, 32(27), 3059–3067. https://doi.org/10.1200/jco.2013.54.8800

HL: Restaging

- All stages with favorable and unfavorable characteristics
- Interim PET-CT completed after 2 cycles of therapy
- Interim restaging is critical to treatment paradigm

References

HL: Restaging

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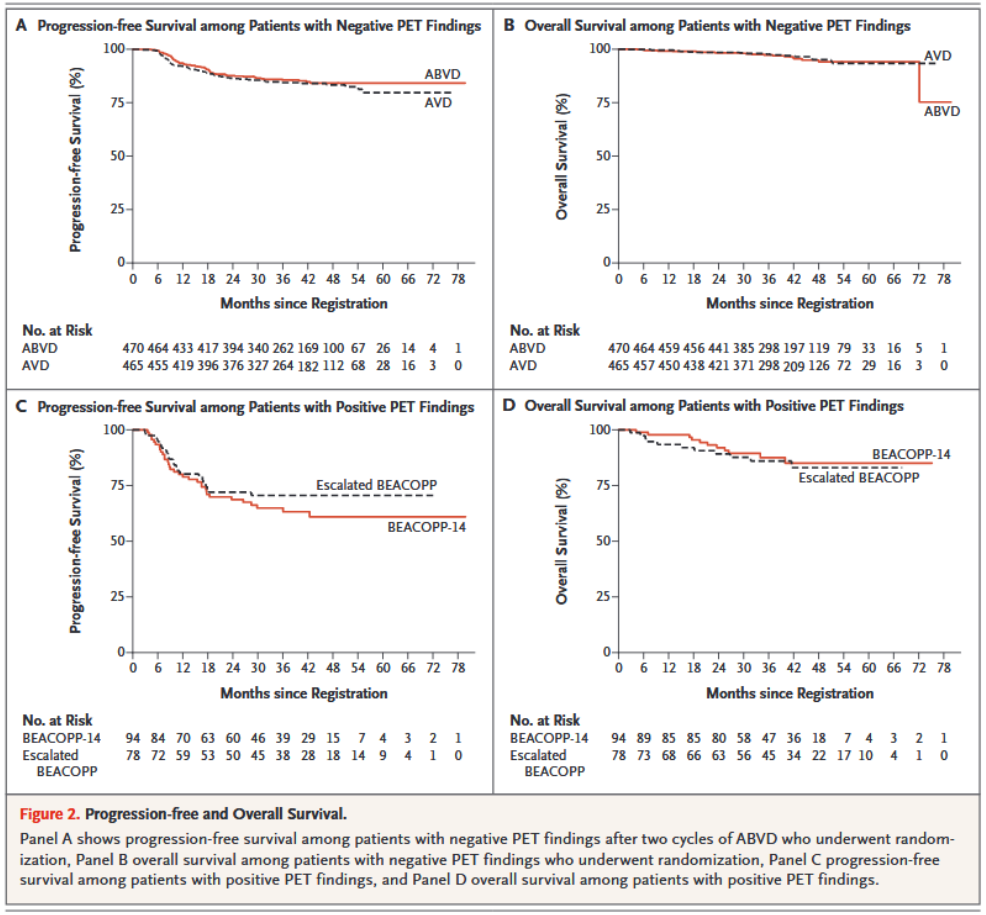

Figure 2. Progression-free and Overall Survival.

Panel A shows progression-free survival among patients with negative PET findings after two cycles of ABVD who underwent randomization, Panel B overall survival among patients with negative PET findings who underwent randomization, Panel C progression-free survival among patients with positive PET findings, and Panel D overall survival among patients with positive PET findings.

Johnson, P., Federico, M., Kirkwood, A., Fosså, A., Berkahn, L., Carella, A., d'Amore, F., Enblad, G., Franceschetto, A., Fulham, M., Luminari, S., O'Doherty, M., Patrick, P., Roberts, T., Sidra, G., Stevens, L., Smith, P., Trotman, J., Viney, Z., … Barrington, S. (2016). Adapted Treatment Guided by Interim PET-CT Scan in Advanced Hodgkin's Lymphoma. The New England Journal of Medicine, 374(25), 2419–2429. https://doi.org/10.1056/nejmoa1510093

References

HL: End of Treatment & Surveillance

- End of Treatment:
  - PET-CT
    - Determine Complete Remission
    - If concerning for primary refractory proceed with biopsy to confirm disease

- Surveillance
  - CT NCAP at 6, 12, and 24 months following treatment or if clinically indicated
  - Routine surveillance with PET is not recommended
  - PET-CT only if last PET was Deauville 4–5, to confirm complete response

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)Hodgkin Lymphoma. 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed August 5, 2020.

References

Hodgkin Lymphoma Case Study

References

Presentation

- 65 year old female initially evaluated PCP for palpable cervical lymphadenopathy
- Medical history is notable for CAD s/p MI, atrial fibrillation and infiltrating mammary carcinoma s/ neoadjuvant TCH and RT, adjuvant trastuzumab and anastrazole
- No B symptoms at time of presentation
- Underwent cervical lymph node biopsy which demonstrated classic Hodgkin Lymphoma, nodular sclerosis type

References

Initial Work Up:

- History and Physical Exam
  - B Symptoms: unexplained fever >101F, drenching night sweats or weight loss >10% of body weight in last 6 months
  - Alcohol intolerance, pruritus, fatigue, performance status, examine lymphoid regions, spleen, liver
- Blood Tests:
  - Completed blood count with differential, inclusive of platelets
  - Comprehensive metabolic panel, inclusive of liver function tests
  - Lactic dehydrogenase
  - May consider Uric Acid if concern for tumor lysis syndrome
  - Erythrocyte sedimentation rate
- Pregnancy testing for women of child bearing age
- Biopsy—excisional preferred for IHC
- PET with CT correlate to evaluate for extent of disease
- Bone marrow biopsy in selected cases
- Infectious work up– HIV, Hepatitis B and C
- Pulmonary function Tests
- Echocardiogram

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)Hodgkin Lymphoma. 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed August 5, 2020.

References

Case: Staging

- CT Chest, Abdomen, Pelvis
  - Multiple enlarged lymph nodes in the right supraclavicular region and upper mediastinum
- Initial PET-CT
  - Deauville PET Criteria=5
    - Multiple FDG avid neck and mediastinal lymph nodes, FDG avid osseous foci in the sacrum and the anterior right acetabulum concerning for osseous metastasis or foci of lymphomatous involvement
- MRI Pelvis
  - Two, small marrow enhancing lesions within the sacrum and right anterior acetabulum, corresponding to FDG avid foci seen on prior PET-CT study; these likely represent osseous metastatic lesions

References

Revised Staging

Table 2. Revised Staging System for Primary Nodal Lymphomas

Stage	Involvement	Extranodal (E) Status
Limited		
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with "bulky" disease	Not applicable
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

NOTE. Extent of disease is determined by positron emission tomography–computed tomography for avid lymphomas and computed tomography for nonavid histologies. Tonsils, Waldeyer's ring, and spleen are considered nodal tissue.

*Whether stage II bulky disease is treated as limited or advanced disease may be determined by histology and a number of prognostic factors.

Cheson, B., Fisher, R., Barrington, S., Cavalli, F., Schwartz, L., Zucca, E., & Lister, T. (2014). Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. Journal of Clinical Oncology, 32(27), 3059–3067. https://doi.org/10.1200/jco.2013.54.8800

Treatment Considerations:

- Definitive pathology→
  Classical Hodgkin lymphoma, mixed cellularity subtype
- Consider Indicators of "Poor Performers":
  - low albumin, high LDH, elevated ESR
- Choice of Chemotherapy Regimen:
  - ABVD vs AAVD vs BEACOPP vs Stanford V
    - Consider cure rate in combination with toxicity profile

References

Considerations for Treatment

- Pulmonary Function Test
  - Pulmonary Toxicity associated with bleomycin
- Echocardiogram
  - Cardiac Toxicity associated with anthracycline
    - Be mindful of lifetime cumulative dose
- Fertility
  - Impact reproductive ability
- Potential Adverse Side Effects:
  - Myelosuppression: neutropenic fever, anemia, bleeding, fatigue, nausea/vomiting, constipation, alopecia, skin changes, peripheral neuropathy

References

Case

- Patient proceeds with treatment with ABVD (adriamycin, bleomycin, vinlblastine, dacarbazine) and completes 2 cycles of chemotherapy without complications

- PET-CT
  - Significant interval decrease in size of multiple lymph nodes within the neck, supraclavicular region and mediastinum.
  - Previously seen FDG avid osseous foci within the sacrum and right acetabulum are no longer seen on this study
  - Deauville 2

References

QUESTION:

- Patient with stage IV Hodgkin Lymphoma completes 2 cycles of ABVD. PET-CT demonstrates interval decrease in lymphadenopathy with Deauville Score 2.
    - How would you counsel patient to anticipate upcoming treatment?

References

Case

- Patient completes 4 cycles of AVD and completes post treatment imaging which demonstrates:
  - CT neck, chest, abdomen, and pelvis demonstrates resolution of previously noted lymphadenopathy
  - PET scored at Deauville 2= Uptake < mediastinum.
- Patient attained a Complete Response (CR)

References

Surveillance

- If complete response as evidence by negative PET, monitoring by hematologist to detect recurrence, late complications of therapy and late relapse is advised
  - Follow up after completion of treatment through 5 years
    - Physical exam, history, laboratory studies
    - CT imaging acceptable at 6, 12, 24 months following treatment or as clinically indicated
    - Counseling should include: reproduction, health habits, psychosocial, cardiovascular, breast self exam, skin cancer
  - Monitoring after 5 years
    - Annual history and physical exam
    - Consider echocardiogram at 10 year intervals
    - Consider site specific screening (i.e. carotid ultrasound with radiation to neck, modified breast screening with chest, axillary radiation
    - Encourage age appropriate health screening
    - Continued counseling on reproduction, health habits, psychosocial, cardiovascular, breast self exam, skin cancer

References

Non-Hodgkin Lymphoma

- Imaging modality is variable for histological subtype
  - FDG avidity is highly variable on subtype
- Staging:
  - PET has established utility in particular subtypes such as diffuse large B cell lymphoma and follicular lymphoma
    - Should be included in staging and may identify best site for biopsy
- Interim Imaging:
  - PET-CT is helpful to determine treatment response
  - Change in therapy only with overt progression
- End of Treatment:
  - PET-CT is standard of care to determine remission in FDG avid lymphoma

Barrington, S., Mikhaeel, N., Kostakoglu, L., Meignan, M., Hutchings, M., Müeller, S., Schwartz, L., Zucca, E., Fisher, R., Trotman, J., Hoekstra, O., Hicks, R., O'Doherty, M., Hustinx, R., Biggi, A., & Cheson, B. (2014). Role of Imaging in the Staging and Response Assessment of Lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group. Journal of Clinical Oncology, 32(27), 3048–3058. https://doi.org/10.1200/jco.2013.53.5229

References

Peripheral T Cell Lymphomas

- Staging:
  - CT chest, abdomen, pelvis
  - CT Neck and MRI brain valuable in certain clinical cases
  - PET has utility due to ability to identify extranodal disease
- Restaging:
  - Interim PET-CT completed after 3-4 cycles of therapy
- End of Treatment
  - PET-CT to determine response to therapy

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)T Cell Lymphomas. 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed August 5, 2020.

References

CLL/SLL

- Staging:
  - CT imaging is not required as part of initial staging and work up
    - Consider if clinically indicated
      - Evaluation of symptoms of bulky disease
  - Consider PET if concern for Richter's transformation
    - Biopsy area with most FDG avidity
- Surveillance
  - Routine use of CT during monitoring is not recommended

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma. 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August 5, 2020.

References