



Response Criteria for Malignant Lymphoma 2007

Cheson Criteria

Quick Reference Guide



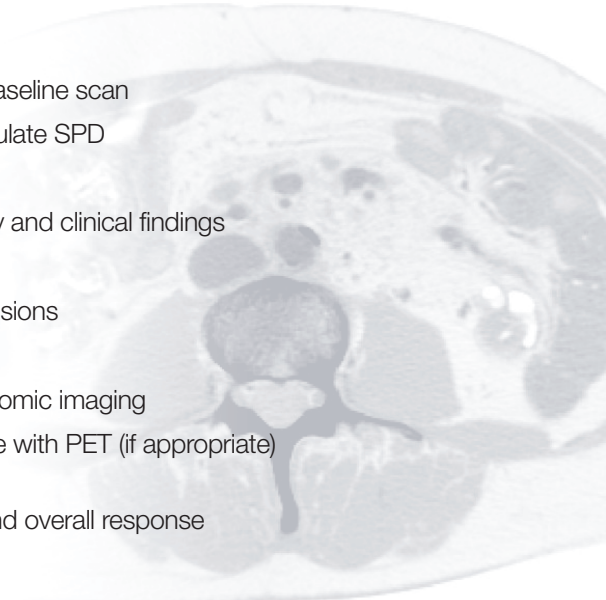
Medical Imaging

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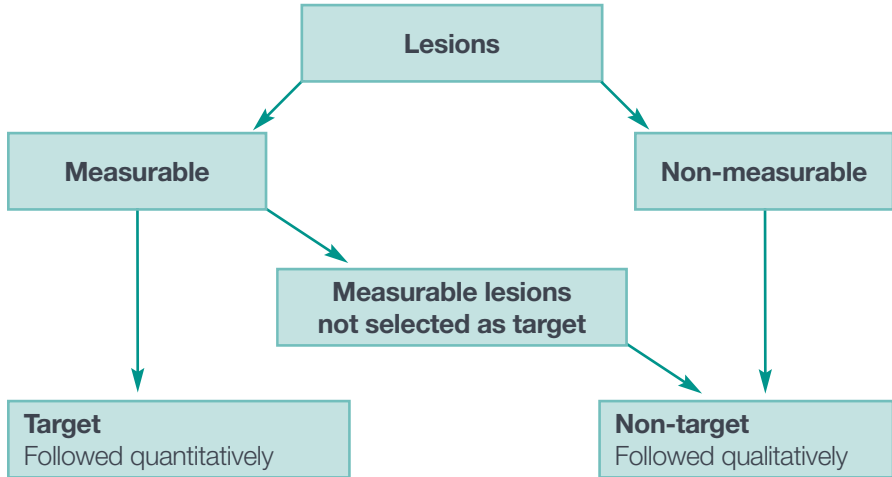
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Summary of Assessments

- Baseline
 - Find all lymphoma lesions on baseline scan
 - Choose target lesions and calculate SPD
 - Consider pre-treatment PET
 - Document bone marrow biopsy and clinical findings
- Subsequent visits
 - Assess target and non-target lesions
 - Search for new lesions
 - Derive response based on anatomic imaging
 - At post-treatment visit, combine with PET (if appropriate) for radiographic response
 - Combine with clinical data to find overall response

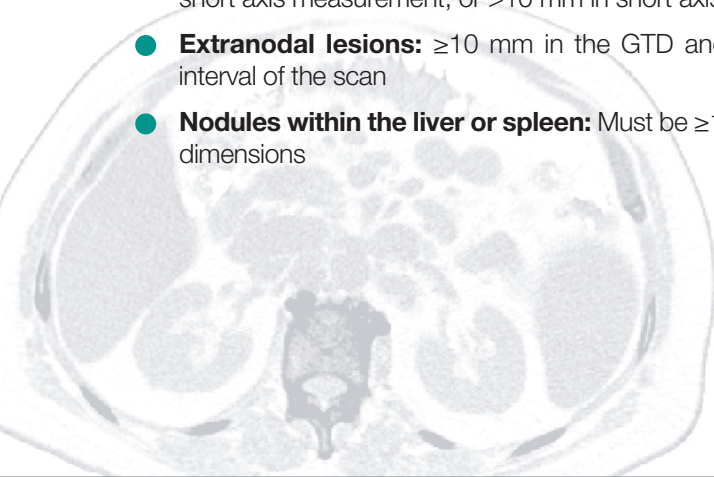


Baseline Lesion Burden



What is a Measurable Lesion?

- Can clearly measure the size in 2 perpendicular dimensions at baseline
- **Nodal lesions:** >15 mm in greatest transverse diameter (GTD) regardless of short axis measurement, or >10 mm in short axis, regardless of the GTD
- **Extranodal lesions:** ≥10 mm in the GTD and twice the reconstruction interval of the scan
- **Nodules within the liver or spleen:** Must be ≥10 mm in two perpendicular dimensions



Choosing Target Lesions

- Select up to 6 lesions
- Larger lesions are preferred
- Lesions should be from disparate regions of the body if possible
- Include mediastinal and retroperitoneal lesions whenever these sites are involved
- Consider reproducibility

Please Remember:

- Record the longest perpendicular diameters (major and minor axes)

Non-Target Lesions

- All other sites of disease present at baseline and not classified as target lesions will be classified as non-target lesions, including any measurable lesions that were not chosen as target lesions

Examples:

- Measurable lesions beyond the maximum number of six
- Bone lesions, irrespective of the modality used to assess them
- Lymphangitis of the skin or lung
- Splenomegaly and hepatomegaly (by CT)
- Groups of lesions that are small and numerous
- Pleural/pericardial effusions and/or ascites
- Irradiated lesions
- Lesions found on physical examination, other than the spleen and liver, that are thought to be malignant (e.g. skin lesions) are non-target lesions
- Can combine multiple lesions in single organ as one entry
 - e.g. “multiple right axillary lymph nodes”

Pre-Treatment FDG-PET

- Strongly recommended for all patients with potentially curable, routinely FDG-avid lymphoma (e.g. Hodgkin's, diffuse large B-cell lymphoma)
 - Negative post-treatment PET is required for CR
 - A negative post-treatment PET can “upgrade” a PR or SD to CR
- For incurable or variably avid lymphoma, pre-treatment PET is recommended only in trials where response rate is a primary trial endpoint

Determining Response

- Assess the CT
 - Measure target lesions and calculate SPD
 - Visually assess non-target lesions
 - Search for new lesions
 - Combine these assessments into the overall CT-based response
- At end of treatment visit, assess PET and combine with CT for overall radiographic response, if appropriate
- Add clinical data (bone marrow, physical exam, b-symptoms) to arrive at overall response for the visit

Target Lesion Response

Complete Remission (CR)	<ul style="list-style-type: none"> ■ Nodes returned to normal (if GTD >15 mm before therapy, GTD now ≤15 mm; if GTD 11-15 and SA >10 mm before therapy, SA now ≤10 mm) ■ All (non-nodal) target lesions completely resolved
Partial Remission (PR)	<ul style="list-style-type: none"> ■ SPD of target lesions decreased ≥50% from baseline ■ Spleen and liver nodules regress by 50% in SPD or single lesion in GTD
Progressive Disease (PD), if after PR or SD, or Relapsed Disease (RD), if after CR	<ul style="list-style-type: none"> ■ SPD increase ≥50% from nadir (smallest value seen during trial) ■ in nodal target lesions overall ■ or in any single nodal target lesion <ul style="list-style-type: none"> ■ A node with SA <10 mm must grow ≥50% and to ≥15 x 15 mm or >15 mm GTD ■ A node with SA >10 mm must increase ≥ 50% in GTD ■ or in non-nodal target lesions overall (e.g. liver/spleen nodules selected as target lesions)
Stable Disease (SD)	<ul style="list-style-type: none"> ■ Not enough shrinkage for PR ■ Not enough growth for PD
Unable to Evaluate (UE)	<ul style="list-style-type: none"> ■ One or more lesions cannot be seen <ul style="list-style-type: none"> ■ This is most commonly caused by inadequate coverage

Special Circumstances

- Target lesion becomes “too small to measure”
 - Non nodal lesion does not disappear, but decreases in size to <5 mm in two dimensions: assign measurements of 5×5 mm for the purpose of calculating the SPD
 - If that lesion increases in size to >5 mm in any dimension afterwards, its actual size should be recorded
- Target lesion splits into two or more smaller lesions:
 - Do not report fragments as “new lesions”
 - Measure each fragment, multiply diameters and add into SPD
- Two lesions merge
 - If both are target lesions, record the products of diameters for the merged lesion for lesion 1, and zero for lesion 2
 - If one lesion is target and one is non-target, the approach should be specified in the trial protocol. Usually, this happens as part of overall progression of disease.

Non-Target Lesion Response

Complete Remission (CR)	<ul style="list-style-type: none">■ All non-target lymph nodes returned to normal size■ All extranodal lesions have completely resolved■ Liver and spleen have returned to normal size (if enlarged at BL)
Stable Disease (SD)	Non-target lesions are still present, but not clearly increased in size
Progressive Disease (PD), if after PR or SD, or Relapsed Disease (RD), if after CR	<ul style="list-style-type: none">■ Unequivocal progression in any non-target lesion<ul style="list-style-type: none">■ A node with SA <10 mm must grow $\geq 50\%$ and to $\geq 15 \times 15$ mm or >15 mm GTD■ A node with SA >10 mm must increase $\geq 50\%$ in GTD
Unable to Evaluate (UE)	One or more lesions cannot be seen

New Lesions

- Any new lesion which measures at least 15 mm in any axis
- Significant new effusions, ascites or other fluid collections, which are radiographically suggestive of malignancy
- New lesions automatically mean progression has occurred
- Be cautious in assessing possible new lesions. If uncertain, re-evaluate at next visit. If the new lesion is confirmed, progression is assigned to the visit when the new lesion was first visible.



“Unable to Evaluate” (UE) Lesion(s)

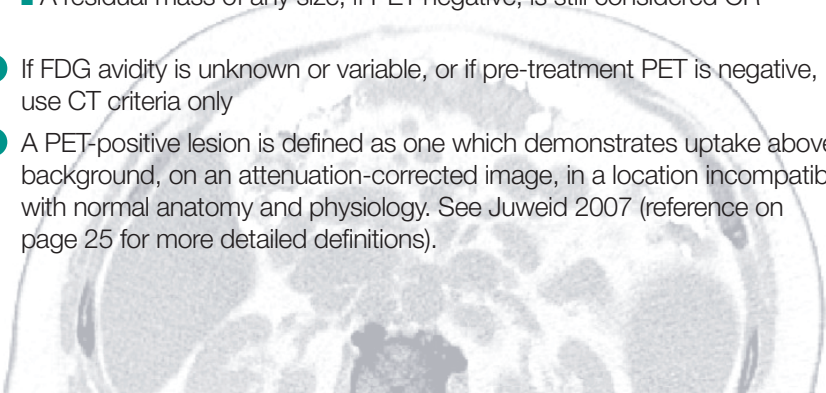
- This category is reserved for target and non-target lesions that are deemed unevaluable (UE) because:
 1. Subsequent (post-baseline) imaging was not performed or did not include the lesion **or**
 2. Lesion(s) could not be evaluated due to poor radiographic technique or poorly defined margins **or**
 3. Lesion(s) identified at baseline were not assessable at a subsequent timepoint

Radiographic Response Based on CT

Target Lesion	Non-Target Lesion	New Lesion	Visit Response
CR	CR	No	CR
CR	SD	No	PR
PR	CR	No	PR
PR	SD	No	PR
SD	CR	No	SD
SD	SD	No	SD
PD	Any	Yes/No	PD
Any	PD	Yes/No	PD
Any	Any	Yes	PD
UE	Any non-PD	No	UE
Any non-PD	UE	No	UE
CR	NA (no non-target lesions identified at baseline)	No	CR
PR		No	PR
SD		No	SD
NA (no target lesions identified at baseline)	SD	No	SD
	CR	No	CR

The Role of PET at End of Treatment

- If the lymphoma is typically FDG avid, or if the pre-treatment PET was positive:
 - Overall radiographic response of CR requires negative PET
 - A response of CR, but with persistently positive PET, is considered PR
 - A residual mass of any size, if PET-negative, is still considered CR
- If FDG avidity is unknown or variable, or if pre-treatment PET is negative, use CT criteria only
- A PET-positive lesion is defined as one which demonstrates uptake above background, on an attenuation-corrected image, in a location incompatible with normal anatomy and physiology. See Juweid 2007 (reference on page 25 for more detailed definitions).



PET Technical Points

- PET is usually performed along with CT (PET/CT) for anatomic coregistration and attenuation correction
 - The CT portion of a PET/CT generally cannot be substituted for a diagnostic CT for the purpose of measuring lesions
- Use PET scans with caution. A variety of pitfalls and artifacts require expert interpretation.
- Special considerations are required for diabetic patients
- Post-treatment PET should be performed no less than
 - 6-8 weeks after chemotherapy
 - 8-12 weeks after radiation

Overall Visit Response

- Combine radiographic and clinical data
 - CT
 - PET
 - Bone marrow
 - Physical exam
 - b-symptoms

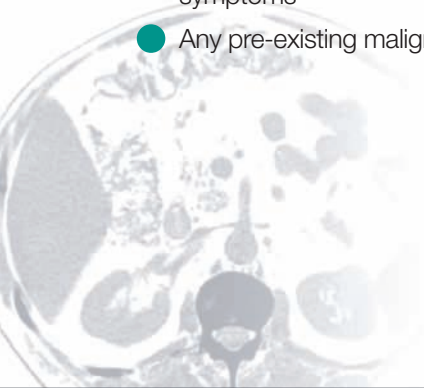


Assessing Response: Bone Marrow

- Lymphoma involvement: Negative – Positive – Indeterminate
- Assess % of lymphocytes in bone marrow aspirate
- Describe pattern of infiltration in bone marrow biopsy
- Bone marrow assessment at end of treatment only required if bone marrow was positive at baseline and the radiographic response is CR
- Once a bone marrow is performed to confirm clearance of the marrow, no further bone marrow evaluation is needed

Complete Remission (CR)

- All nodal and non-nodal lesions disappeared
- PET (if used) negative
- No palpable hepatosplenomegaly or other physical exam findings
- Complete disappearance of clinical evidence of disease and disease-related symptoms
- Any pre-existing malignancy cleared on repeat bone marrow biopsy



Complete Remission (CR) cont.

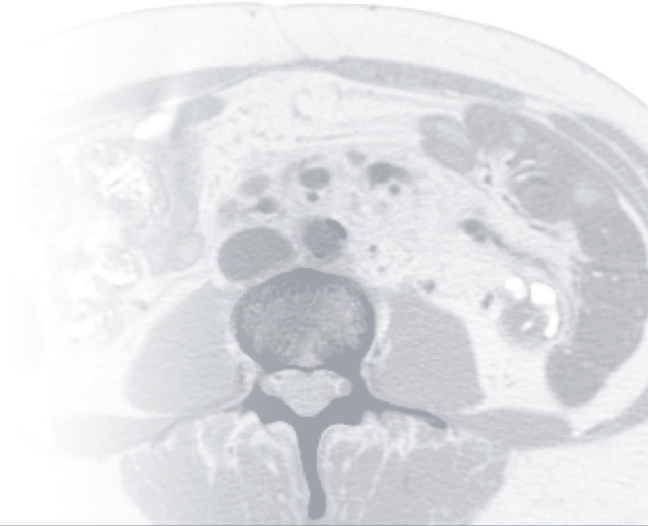
- Details of bone marrow biopsy requirements
 - Biopsy sample must be adequate (>20 mm unilateral core)
 - **If indeterminate by morphology, the sample should be negative by immunohistochemistry**
 - A sample that is negative by immunohistochemistry but demonstrating a small population of clonal lymphocytes by flow cytometry will be considered a CR until data become available demonstrating a clear difference in patient outcome
 - In patients with splenic MZL, normalization of the blood counts (Hgb >12 g/dL; platelets >100 x 10⁹/L; neutrophils >1.5 x 10⁹/L and no circulating clonal B cells) required.
 - In patients with extranodal (MALT) MZL with gastric involvement at screening, response assessed with both endoscopy and histology. Complete histologic regression occurs when post-treatment biopsies show no macroscopic lymphoma but instead an empty tunica propria with small basal clusters of lymphocytes and scattered plasma cells.

Partial Remission (PR)

- PR by CT
 - $\geq 50\%$ reduction in target lesions, no growth of non-target or new lesions
- If PET used, PET positive in at least one previously involved lesion
 - CR by CT, but with persistent positive PET is PR
- If imaging response is CR, but there is persistent bone marrow involvement, the overall response is PR
 - If positive, cell type should be specified (e.g. large-cell lymphoma or small neoplastic B cells)
- If imaging response is CR, but there is persistent clinical evidence of disease on physical exam (hepatosplenomegaly, neck masses, skin lesions) or b-symptoms, the overall response is PR

Stable Disease (SD)

- Failing to attain the criteria needed for a CR or PR, but not fulfilling those for progressive disease



Relapsed Disease (RD; after CR) or Progressive Disease (PD; after PR or SD)

- Increased disease burden seen on anatomic imaging as defined above
 - $\geq 50\%$ increase from nadir in SPD of target lymph nodes, **or** single involved node **or** the size of other lesions (e.g., splenic or hepatic nodules)
 - A lymph node with SA < 10 mm must increase by $\geq 50\%$ and to a size of 15×15 mm or more than 15 mm in the GTD
 - A previously identified abnormal lymph node > 10 mm in short axis must increase by $\geq 50\%$ in GTD
- Appearance of new abnormal nodes or any new lesion > 15 mm in any axis
 - New FDG-positive site is only PD if confirmed with other modalities
- Clinical signs and symptoms alone cannot be called progression using these criteria

References

Print Version:

“Revised Response Criteria for Malignant Lymphoma.” *Journal of Clinical Oncology*, Volume 25, No 5, (February 10), 2007: pp. 579-586.

“Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma.” *Journal of Clinical Oncology*, Volume 25, No 5, (February 10), 2007: pp. 571-578.

Online Version: <http://jco.ascopubs.org/content/25/5/579.abstract>



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