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Basic Paradigm

- Assess at baseline
  - Look for measurable lesions
  - Select target and non-target lesions
  - Measure target lesions
  - Add up to get tumor burden
- Treat patient
- Follow-up evaluation
  - Measure target lesions
  - Assess non-target lesions and look for new lesions
  - Calculate timepoint response
Image Acquisition

- CT
  - Slice thickness ≤5mm if possible, contiguous
  - IV and oral contrast used (3-phase liver if appropriate)
  - Field of view adjusted to body habitus (include the whole body, out to the skin)

- MRI
  - Axial T1 and T2, axial T1 post contrast
  - ≤5mm contiguous slices if possible
  - Use the same machine for all timepoints

- PET/CT
  - Not required, but may be useful for assessment of new lesions on future timepoints (see page 18)
  - CT portion of PET/CT is usually of lower quality, and should not be used instead of dedicated diagnostic CT. If the CT is of high quality, with oral and IV contrast, use with caution. Additional information from PET may bias CT assessment.
  - Use the same machine for all timepoints

- Calipers – Hard to use reproducibly
  - Include ruler in photograph for skin lesions

- Chest x-ray (CXR) – Use CT instead (if possible)

- Ultrasound – Not reproducible
Measurable Lesions

- Tumor ≥10 mm in longest diameter (LD) on an axial image on CT or MRI with ≤5 mm reconstruction interval
  - If slice thickness >5 mm, LD must be at least 2 times the thickness
- Tumor ≥20 mm LD by chest x-ray (if clearly defined & surrounded by aerated lung); CT is preferred (even without contrast)
- Tumor ≥10 mm LD on clinical evaluation (photo) with electronic calipers; skin photos should include ruler
  - Lesions which cannot be accurately measured with calipers should be recorded as non-measurable
- Lymph nodes ≥15 mm in short axis on CT (CT slice thickness no more than 5 mm)
- Ultrasound cannot be used to measure lesions
Non-Measurable Lesions

- All other definite tumor lesions
  - Masses <10 mm
  - Lymph nodes 10-14 mm in short axis
  - Leptomeningeal disease
  - Ascites, pleural or pericardial effusion
  - Inflammatory breast disease
  - Lymphangitic involvement of skin or lung
  - Abdominal masses or organomegaly identified by physical exam which cannot be measured by reproducible imaging techniques

- Benign findings are NEVER included. Also, do not include equivocal (“cannot exclude”) findings
Special Lesion Types

- **Bone Lesions**
  - NMBS, PET scans & plain films can be used to confirm the presence or disappearance of bone lesions, but NOT for measurement.
  - Bone lesions with identifiable soft tissue components seen on CT or MR can be measurable if the soft tissue component meets the definition above.
  - Blastic bone lesions are unmeasurable.

- **Cystic Lesions**
  - Simple cysts are not included as lesions.
  - Cystic metastases may be selected, but prefer to use non-cystic lesions as "target".
  - Clarify with sponsor as to their acceptability before study start.
Baseline Lesion Burden

Lesions

Measurable

Measureable lesions not selected as target

Target
Followed quantitatively

Non-measurable

Non-target
Followed qualitatively

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**Target Lesions**

- Choose up to 5 lesions
  - Up to 2 per organ
- Add up longest diameters (LD) of non-nodal lesions (axial plane)
- Add short axis diameters of nodes
- This is the “sum of the longest diameters” (SLD)
Baseline Documentation

Only patients with measurable disease at baseline should be included in protocols where objective tumor response is the primary endpoint.

- **Target Lesions**
  - A maximum of five (5) target lesions in total (up to two (2) per organ)
  - Select largest reproducibly measurable lesions
  - If the largest lesion cannot be measured reproducibly, select the next largest lesion which can be

- **Non-Target Lesions**
  - It is possible to record multiple non-target lesions involving the same organ as a single item on the eCRF (e.g. “multiple enlarged pelvic lymph nodes” or “multiple liver metastases”)
Lesions with Prior Local Treatment

- Lesions in previously irradiated areas (or areas treated with local therapy) should not be selected as target lesions, unless there has been demonstrated progression in the lesion.
- Conditions in which these lesions would be considered target lesions should be defined in study protocols.
Evaluating Response at Each Timepoint

- Measure previously chosen target lesions
  - Even if they are no longer the largest
- Evaluate all previously identified non-target lesions
- Look for new definite cancer lesions
**Target Lesion Evaluation**

- Measure LD (axial plane) for each target lesion
- Measure short axis for target lymph nodes
- Add these measurements to get the SLD
- If too small to measure, a default value of 5 mm is assigned.
  If the lesion disappears completely, the measurement is recorded as 0 mm.

- Splitting or coalescent lesions
  - If a target lesion fragments into multiple smaller lesions, the LDs of all fragmented portions are added to the sum
  - If target lesions coalesce, the LD of the resulting coalescent lesion is added to the sum
# Target Lesion Evaluation

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>Disappearance of all extranodal target lesions. All pathological lymph nodes must have decreased to &lt;10 mm in short axis.</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>At least a 30% decrease in the SLD of target lesions, taking as reference the baseline sum diameters</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>SLD increased by at least 20% from the smallest value on study (including baseline, if that is the smallest) The SLD must also demonstrate an absolute increase of at least 5 mm. (Two lesions increasing from 2 mm to 3 mm, for example, does not qualify)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD</td>
</tr>
</tbody>
</table>
## Non-Target Lesion Evaluation

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>- Disappearance of all extranodal non-target lesions</td>
</tr>
<tr>
<td></td>
<td>- All lymph nodes must be non-pathological in size (&lt;10 mm short axis).</td>
</tr>
<tr>
<td></td>
<td>- Normalization of tumor marker level</td>
</tr>
<tr>
<td>Non CR/Non PD</td>
<td>Persistence of one or more non-target lesion(s) and/or maintenance of</td>
</tr>
<tr>
<td></td>
<td>tumor marker level above the normal limits</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>Unequivocal progression of existing non-target lesions. (Subjective</td>
</tr>
<tr>
<td></td>
<td>judgement by experienced reader)</td>
</tr>
</tbody>
</table>
New Lesions

- Should be unequivocal and not attributable to differences in scanning technique or findings which may not be a tumor
  - Does not have to meet criteria to be “measurable”

- If a new lesion is equivocal, continue to next timepoint. If confirmed then, PD is assessed at the date when the lesion was first seen.

- Lesions identified in anatomic locations not scanned at baseline are considered new

- New lesions on US should be confirmed on CT/MRI
FDG-PET

- **New lesions can be assessed using FDG-PET**
  - A ‘positive’ FDG-PET scan lesion means one with uptake greater than twice that of the surrounding tissue on the attenuation corrected image.
  - (-) PET at baseline and (+) PET at follow-up: Progressive Disease (PD) based on a new lesion.
  - No PET at baseline and (+) PET at follow-up: PD if the new lesion is confirmed on CT. If a subsequent CT confirms the new lesion, the date of PD is the date of the initial PET scan.
  - No PET at baseline and (+) PET at follow-up corresponding to a pre-existing lesion on CT that is not progressing is **not** PD.
**Missing Assessments and Non-evaluable Designation**

- If all lesions cannot be evaluated due to missing data or poor image quality the patient is not evaluable (NE) at that time point.

- If only a subset of lesions can be evaluated at an assessment, the visit is also considered NE, unless a convincing argument can be made that the contribution of the individual missing lesion(s) would not change the assigned time point response.
  
  E.g. PD based on other findings.
Recurrence of Lesions

- For a patient with Stable Disease (SD)/Partial Response (PR), a lesion which disappears and then reappears will continue to be measured and added to the sum
  - Response will depend on the status of the other lesions
- For a patient with Complete Response (CR), reappearance of a lesion would be considered Progressive Disease (PD)
Evaluation of Overall Timepoint Response for Patients with Measurable Disease at Baseline

<table>
<thead>
<tr>
<th>Target Lesions</th>
<th>Non-Target Lesions</th>
<th>New Lesions</th>
<th>Overall Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>CR</td>
<td>No</td>
<td>CR</td>
</tr>
<tr>
<td>CR</td>
<td>Non-CR/Non-PD</td>
<td>No</td>
<td>PR</td>
</tr>
<tr>
<td>CR</td>
<td>NE</td>
<td>No</td>
<td>PR</td>
</tr>
<tr>
<td>PR</td>
<td>Non-PD or NE</td>
<td>No</td>
<td>PR</td>
</tr>
<tr>
<td>SD</td>
<td>Non-PD or NE</td>
<td>No</td>
<td>SD</td>
</tr>
<tr>
<td>Not all evaluated</td>
<td>Non-PD</td>
<td>No</td>
<td>NE</td>
</tr>
<tr>
<td>PD</td>
<td>Any</td>
<td>Yes or No</td>
<td>PD</td>
</tr>
<tr>
<td>Any</td>
<td>PD</td>
<td>Yes or No</td>
<td>PD</td>
</tr>
<tr>
<td>Any</td>
<td>Any</td>
<td>Yes</td>
<td>PD</td>
</tr>
</tbody>
</table>

CR = Complete Response, PR = Partial Response, SD = Stable Disease, PD = Progressive Disease, NE = Not Evaluable
## Evaluation of Overall Timepoint Response for Patients without Measurable Disease at Baseline

<table>
<thead>
<tr>
<th>Non-Target</th>
<th>New</th>
<th>Overall Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>No</td>
<td>CR</td>
</tr>
<tr>
<td>Non-CR/Non-PD</td>
<td>No</td>
<td>Non-CR/Non-PD</td>
</tr>
<tr>
<td>Not all evaluated</td>
<td>No</td>
<td>NE</td>
</tr>
<tr>
<td>Unequivocal Progression</td>
<td>Yes or No</td>
<td>PD</td>
</tr>
<tr>
<td>Any</td>
<td>Yes</td>
<td>PD</td>
</tr>
</tbody>
</table>

**CR = Complete Response, PD = Progressive Disease, NE = Not Evaluable**
Confirmation

- Confirmation of Partial Response (PR)/Complete Response (CR) is only required for non-randomized trials where response is the primary endpoint.

- In these trials, subsequent confirmation of PR with one interim time point of Stable Disease (SD) is acceptable.
## What Has Changed: RECIST 1.0 – RECIST 1.1

<table>
<thead>
<tr>
<th></th>
<th>RECIST 1.0</th>
<th>RECIST 1.1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumor Burden</strong></td>
<td>10 Targets (5 per organ)</td>
<td>5 Targets (2 per organ)</td>
</tr>
<tr>
<td><strong>Lymph Nodes</strong></td>
<td>Measure like any other lesion</td>
<td>Measure short axis</td>
</tr>
<tr>
<td></td>
<td>Defined normal size</td>
<td>Defined normal size</td>
</tr>
<tr>
<td><strong>PD Definition</strong></td>
<td>20% increase in SLD</td>
<td>20% increase in SLD</td>
</tr>
<tr>
<td></td>
<td>5 mm absolute increase</td>
<td>5 mm absolute increase</td>
</tr>
<tr>
<td><strong>Non-measurable PD</strong></td>
<td>“Unequivocal”</td>
<td>More details and examples</td>
</tr>
<tr>
<td><strong>Confirmation</strong></td>
<td>Required for PR and CR</td>
<td>Required in non-randomized</td>
</tr>
<tr>
<td></td>
<td></td>
<td>trial with response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>as 1º endpoint</td>
</tr>
<tr>
<td><strong>New Lesions</strong></td>
<td></td>
<td>Section on FDG-PET</td>
</tr>
</tbody>
</table>
Modifications and Variants

- RECIST is not set in stone
- Modifications for specific disease processes have been documented
- Modifications may be made to meet the needs of individual trials
References

Print Version:


**Online Version:** http://www.eortc.be/Recist/Default.htm
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