Tumor Response Assessment in Adult Clinical Trials

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Objectives: To discuss-

• Conventional imaging response criteria
  – RECIST 1.1
  – Advantages and limitations

• Enabling use of response criteria with multimedia reports
Why Tumor Response Criteria

- It remains critically important to the conduct and outcome of clinical trials
- Need to be able to compare results across non-randomized clinical trials
- Need to be able to compare results among sites within a clinical trial
Why Tumor Response Criteria

- In clinical reads, radiologists usually describe tumors subjectively and often ambiguously,
- Lesion measurements are not recorded in a format that permits reproducibility, making it difficult to evaluate response
New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1) 2009

RECIST 1.1

- Three components:
  - Target lesion evaluation
  - Non-target lesion evaluation
  - New lesion detection
- CT scan preferred imaging modality
- MRI can be substituted
- NO ultrasound
- Reconstruction slice thickness ≤ 5mm
RECIST 1.1 Target Lesions

• **Choose**
  – up to 2 lesions per organ
  – up to 5 lesions total
• Non-nodal lesions long axis > 1.0 cm
• Lymph nodes short axis ≥ 1.5
• Bone lesions with a lytic component and measurable soft tissue mass
Example: Non-nodal Target Lesions

- Must be > 10 mm long axis
- Two lesions can be target lesions
- Measure in axial plane in longest dimension
Reproducible Defined Margins

Sharp margins
Ideal to measure

Irregular margins

Imperceptible margins

Reproducible measurements unlikely

Jaffe J Clin Oncol 2006; 24:3245
Liver Lesions as Target Lesions

- The rim should be included in the measurements
- View at liver windows

Van Meerten Eur Radiol 2010; 20:1456-1467
RECIST 1.1

IV contrast is mandatory
If there is no IV contrast at baseline, cannot assess full tumor burden or response
RECIST 1.1 Lymph Node Assessment

- **Measure SHORT axis** (not long axis)
  - > 15 mm: target lesion status
  - 10 to <15 mm: non-target
  - < 10 mm: normal
Measuring Lymph nodes
Ex: Lymph Node Measurement
Lung Cancer

2 cm Target lesion

9 mm normal

Courtesy L Schwartz
Lymph Node Specifications

0.7 cm normal

1.6 mm abnormal
Specifications on Bone Lesions

- Bone lesions may be target lesions if they are either lytic or mixed lytic-blastic with a soft tissue component that meets criteria for measurability.
  - PET, bone scintigraphy, or radiography cannot be used when measuring disease response.

- Blastic bone lesions are non-measurable.
Bone Lesions as Target Lesions

Non-Target blastic

Measurable ST component

Chalin et al RadioGraphics 2011; 31:2093-2105
What Should NOT be a Target Lesion?

• Non-nodal lesions < 10 mm in longest diameter
• Nodes 10 to <15 mm in short axis
• Lesions with poorly visualized margins
• Bone lesions without measurable components
• Previously irradiated lesions
• Blastic bone lesions

THESE CAN BE NON-TARGET LESIONS
DO NOT MEASURE
Non-Target Lesions

- 9mm nodule
- Poorly defined margins
- Nodes 10 to <15 mm

Van Meerten Eur Radiol 2010; 20:1456-1467
Non-Target Lesions

Multiple small nodules

Lymphangitic spread
What is totally excluded from imaging response assessment

- These are **not recorded** at baseline or followed
  - Nodes <1 cm in short diameter ("normal")
  - Pleural/pericardial effusion/ascites
  - Simple cysts
Follow Up Evaluation

• Evaluate same components at each time point
  – Target lesions (quantitative)
    » even if they are no longer the largest
  – Non-target lesions (qualitative)
• Look for new definite lesions
Target Lesion Measurements at Follow Up

- Use the same Baseline Window Level at all follow up examinations
Target Lesion Measurements at Follow Up

- Choose the slice where the target lesion is largest, even if it is different from baseline
Target Lesion Measurements at Follow Up

- Add the measurements of all target lesions at baseline and follow-up to get Sum of diameters (SOD)
  - Calculate % change from Baseline or Nadir
    » % change determines the response
Target Lesion Response: PR

Baseline
SOD = 10 cm

Follow up
SOD = 6 cm

- 40% decrease in SOD \(((10 - 6 \text{ cm}) / 10 \text{ cm} \times 100) = \text{ PR}\)

Nishino AJR:195, August 2010
Non-Target Lesions at Follow Up

• There is no size criteria

• Evaluate these qualitatively and record status as absent, present, or unequivocal progression

• Note: Unequivocal progression in non-target lesions should be selected only when the disease burden has increased to the level where the study drug should be discontinued, even if there is stable disease or a partial response in the target lesions
New Lesions

- New lesions are reported as “yes” or “no”
- Should be unequivocal
  - i.e., represent malignant disease rather than a benign process and is not due to difference in scanning technique

When in doubt continue treatment, repeat evaluation, including with FDG-PET
Unequivocal PD
New Liver metastases
New Liver Lesion – Equivocal Does Not Mandate PD

7mm
Finally, Evaluate Overall Response
RECIST 1.1 Categories for Response of Target Lesions

- CR = complete response
- PR = partial response
- PD = progressive disease
- SD = stable disease
Evaluate All Lesions in Combination Target, Non-target and New Lesions

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>Target and non-target lesions resolved, nodes &lt; 10 mm</td>
</tr>
<tr>
<td>PR</td>
<td>&gt;30% decrease SOD of Target Lesions AND Non-target are non-PD</td>
</tr>
<tr>
<td>PD</td>
<td>➢ 20% increase SOD of target lesions AND ≥5 mm absolute increase from nadir OR ➢ Non-target progress OR New lesions</td>
</tr>
<tr>
<td>SD</td>
<td>Does not meet PR or PD</td>
</tr>
</tbody>
</table>

CR = complete response; PR = partial response; PD = progressive disease; SD = stable disease
Challenge in tumor response assessment is how to collect, record and communicate the data.
Dedicated Automated Software

• Accessible from existing PACS workstation or web browser
• Quantitative measurement tools for variety of response criteria
  – RECIST, irRECIST, mRECIST, Cheson, Lugano, Rano
• Assesses response with automatic response classification
• Compares to nadir, baseline and prior time points
• Automated report communication
Automated Technology
Target Lesions
Automated Technology
Target Lesions

T02 Omental nodule
Name: Omental nodule
Category: Target

Organ: Omentum
State: Present

Size:
Long axis: 18.5 mm
Automated Technology
Non-target Lesions
## Automated Report: Baseline

<table>
<thead>
<tr>
<th>Lesion name</th>
<th>Baseline (04/04/2016 (CT), 04/19/2016 (CT))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target lesions</strong></td>
<td></td>
</tr>
<tr>
<td>1 T01 Pancreatic mass</td>
<td>LA: 3.5 cm (CT: SE 5; IN 108; TP -399)</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
</tr>
<tr>
<td>2 T02 Omental nodule</td>
<td>LA: 1.8 cm (CT: SE 5; IN 120; TP -423)</td>
</tr>
<tr>
<td>Omentum</td>
<td></td>
</tr>
<tr>
<td><strong>Non-target lesions</strong></td>
<td></td>
</tr>
<tr>
<td>1 NT01 omental nodularity</td>
<td>State: Present</td>
</tr>
<tr>
<td>Omentum</td>
<td></td>
</tr>
<tr>
<td>2 NT02 Retroperitoneal nodes</td>
<td>State: Present</td>
</tr>
<tr>
<td>Lymph node</td>
<td></td>
</tr>
<tr>
<td><strong>Target sum</strong></td>
<td>5.3 cm</td>
</tr>
</tbody>
</table>

**Evaluation**

- Target response
- Non-target response
- New lesions present
- Timepoint response
## Automated Report: Follow-up

<table>
<thead>
<tr>
<th>Lesion name</th>
<th>Baseline (04/04/2016 (CT), 04/19/2016 (CT))</th>
<th>Follow-up 1 (06/20/2016 (CT))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target lesions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 T01 Pancreatic mass</td>
<td>LA: 3.5 cm (CT: SE 5; IN 108; TP -399)</td>
<td>LA: 3.4 cm (CT: SE 3; IN 185; TP -859.5)</td>
</tr>
<tr>
<td>2 T02 Omental nodule</td>
<td>LA: 1.8 cm (CT: SE 5; IN 120; TP -423)</td>
<td>State: Disappeared</td>
</tr>
<tr>
<td><strong>Non-target lesions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 NT01 omental nodularity</td>
<td>State: Present</td>
<td>State: Disappeared</td>
</tr>
<tr>
<td>2 NT02 Retroperitoneal nodes</td>
<td>State: Present</td>
<td>State: Present</td>
</tr>
<tr>
<td><strong>Target sum</strong></td>
<td>5.3 cm</td>
<td>3.4 cm</td>
</tr>
<tr>
<td><strong>Evaluation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target response</td>
<td>Partial Response</td>
<td></td>
</tr>
<tr>
<td>Non-target response</td>
<td>Non-CR/Non-PD</td>
<td></td>
</tr>
<tr>
<td>New lesions present</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Timepoint response</td>
<td>Partial Response</td>
<td></td>
</tr>
</tbody>
</table>
Automated Technology
Multimedia Reporting

Graphical overview (target sum)

Lesion overview chart

T01 Pancreatic Mass
Pancreas

Size

Pancreatic Target Lesion
Thank you!