RECIST 1.1 and SWOG Protocol Section 10

Louise Highleyman, Data Coordinator

SWOG Statistics and Data Management Center

Response Evaluation Criteria in Solid Tumors (RECIST) 1.1

- 2009: Revised RECIST guideline (1.1) published in the *European Journal of Cancer*
- The same year, S0905 becomes first SWOG study to use RECIST 1.1 in study endpoint
- Now used in most SWOG solid tumor protocols
- Major changes from RECIST 1.0:
  - Criteria for evaluating lymph nodes in CR
  - Number of target lesions (5 total, 2 per organ)
  - Guidance on new lesions (PD)
  - Clarifications and notes on FAQ's

SWOG Protocol Section 10

- In every protocol: **Criteria for Evaluation and Endpoint Analysis**

- For most solid tumor studies, summary of RECIST 1.1 criteria:
  - Measurability of Lesions
  - Objective Status at Each Disease Evaluation
  - Best Response

Refinements to RECIST 1.1

- Since 2009, there have been manuscripts and FAQs that provide clarification and refinements to RECIST 1.1

- Check out the RECIST Working Group's website at http://recist.eortc.org/ for this information

Edits to Protocol Section 10

- Whole body scanning
- Slice thickness
- What counts as an organ when selecting two target lesions?
  - Lymph nodes
  - Paired organs
  - Pleura vs. lungs
- Lymph nodes and progression
- Equivocal progression findings

Edits to Protocol Section 10: Whole Body Scanning

- If study uses disease progression as an endpoint:
  - All potential sites of metastases should be evaluated at each time point
  - Acceptable: only the areas most likely to be involved with metastatic disease for the tumor type, plus any areas with suspected involvement based upon clinical symptoms

Edits to Protocol Section 10: Slice Thickness

- The defined measurability of lesions on CT scan is based on the assumption that CT slice thickness is 0.5 cm or less.

- It is strongly recommended that CT slice of 5 mm or less be used.

- This also applies to the CT portion of a PET-CT (must be identical diagnostic quality to diagnostic CT)

Edits to Protocol Section 10: Two Target Lesions Per Organ

- Lymph nodes are considered one organ
  - Only two lymph nodes should be selected as target lesions.
- “Paired” organs are considered one organ
  - I.e.: lungs, kidneys and ovaries
- Pleural-based lung lesions are considered part of the lung in determining target lesions
  - Pleural effusions/thickening can be reported as a separate site.

Edits to Protocol Section 10: Lymph Nodes and Progression

- Refresher on how RECIST 1.1 deals with lymph nodes
  - At baseline:
    - LNs <1.0 cm in short axis = **non-pathological**, should not be recorded or followed
    - LNs ≥ 1.0 cm and < 1.5 cm in short axis: abnormal (pathologically enlarged) and **non-measurable**
    - LNs ≥ 1.5 cm in short axis: abnormal (pathologically enlarged) and **measurable**
  - In setting of Complete Response:
    - All lymph nodes (target & non-target) must be <1.0 cm in short axis

Edits to Protocol Section 10: Lymph Nodes and Progression

- What if:
  - A non-target lymph node (SA between 1.0 and 1.5 cm at baseline) becomes normal (SA < 1.0 cm) and then recurs (SA ≥ 1.0 cm)?
    - Must meet the criteria for PD based on non-target lesions (“unequivocal progression”) to be considered PD

Edits to Protocol Section 10: Lymph Nodes and Progression

- What if:
  - A target lymph node (SA ≥ 1.5 cm at baseline) becomes normal (SA < 1.0 cm) and then grows back to SA ≥ 1.5 cm?
    - Should be added to the sum of diameters to determine if criteria for PD are met

Edits to Protocol Section 10: Lymph Nodes and Progression

- What if?
  - A normal lymph node at baseline (SA <1.0 cm) becomes pathologic (SA ≥ 1.0 cm)?
    - This LN is considered a new lesion and should be considered PD

Edits to Protocol Section 10: Lymph Nodes and Progression

- If a single pathologic lymph node is driving the progression event:
  - Continuation of treatment/follow-up and confirmation by a subsequent exam should be contemplated.
  - If it the newly pathologic lymph node does not resolve, or increases in size, this confirms PD
  - The date of progression would be the date the “new” lymph node was first documented.

Edits to Protocol Section 10: Equivocal Progression Findings

- Equivocal findings of progression include:
  - very small and uncertain new lesions
  - cystic changes
  - necrosis in existing lesions
- Treatment may continue until the next scheduled assessment
- If at the next scheduled assessment, PD is confirmed, the date of progression should be the earlier date when progression was suspected.

RECIST Tips & Suggestions

- Be sure to read the protocol carefully for any study-specific endpoints or modifications to standard RECIST

- All sites of disease present at baseline should be listed on Baseline Tumor Assessment (either target or non-target disease)
  - Otherwise, we can't tell if patient truly achieves a complete response (CR)

RECIST Tips & Suggestions

- Use a RECIST tracking log or similar source document
  - Do not rely on the dictated radiology report alone
- Have the same person (radiologist or investigator) provide measurements each time

RECIST Tips & Suggestions

- When in doubt, ask!
  - BreastQuestion@crab.org
  - GIQuestion@crab.org
  - GUQuestion@crab.org
  - LungQuestion@crab.org
  - MelanomaQuestion@crab.org
  - RareTumors@crab.org

References

- The RECIST Working Group's website: http://recist.eortc.org/

- Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. **New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1).** Eur J Cancer. 2009 Jan;45(2):228-47. doi: 10.1016/j.ejca.2008.10.026. PubMed PMID: 19097774.

- Schwartz LH, Bogaerts J, Ford R, Shankar L, Therasse P, Gwyther S, Eisenhauer EA. **Evaluation of lymph nodes with RECIST 1.1.** Eur J Cancer. 2009 Jan;45(2):261-7. doi: 10.1016/j.ejca.2008.10.028. Epub 2008 Dec 16. PubMed PMID: 19091550.

- Schwartz LH, Litière S, de Vries E, Ford R, Gwyther S, Mandrekar S, Shankar L, Bogaerts J, Chen A, Dancey J, Hayes W, Hodi FS, Hoekstra OS, Huang EP, Lin N, Liu Y, Therasse P, Wolchok JD, Seymour L. **RECIST 1.1-Update and clarification: From the RECIST committee.** Eur J Cancer. 2016 Jul;62:132-7. doi: 10.1016/j.ejca.2016.03.081. Epub 2016 May 14. PubMed PMID: 27189322; PubMed Central PMCID: PMC5737828.