

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

RESPONSE ASSESSMENT

Response to therapy is the primary endpoint of most Phase II studies and a secondary endpoint of some Phase III studies. To assess a patient's response to therapy correctly, we must have accurate tumor assessment on all lesions as well as complete information for graphic studies (X-rays, scans, etc.) and laboratory tests used for response evaluation. Phase II studies, by design, have small sample sizes and terminate early when few or no responses are observed. Thus, these studies are particularly sensitive to errors in recording response factors. Incorrect response assessment may result in needless exposure of patients to an ineffective agent, early study closure, incorrectly labeling an agent as ineffective, or a biased response rate estimate.

Specific criteria for assessing response are found in Section 10 of each protocol. Evaluating response requires that both pre-treatment and subsequent disease assessments are performed at intervals specified in the protocol Study Calendar, found in Section 9 of the protocol as well as Section 7 in some studies. Response is documented on protocol-specific forms. All data forms are submitted online, however, copies of study forms are available on the Protocol Abstract page at www.swog.org and on CTSU under the “Documents” tab and “Protocol Related Documents” subtab. These may be used as worksheets in preparation for online data entry. Response assessment is only possible when all sites of disease are reviewed and disease extent is recorded accurately.

General guidelines for assessing both solid tumor and hematologic cancers:

1. **Always** use the response criteria and schedule given in Section 10 of the protocol.
2. **Every** disease assessment called for in Section 7 and on the study calendar in Section 9 must be done and done on time.
3. **All disease** present at baseline must be documented to ensure that response can be properly assessed.
4. **Each site** of disease must be assessed at every scheduled disease assessment, unless otherwise specified in the study protocol.
5. The **same method** of measuring the disease used at baseline must be used at each assessment.
6. Usually a **confirmation assessment** is required after an initial observation of response. It should be scheduled according to the protocol instructions.

10.0 Criteria for Evaluation and Endpoint Definitions

10.1 Measurability of lesions:

- **Measurable disease**

Measurable disease is defined differently for lymph nodes compared with other disease and will be addressed in a separate section below.

- Lesions that can be accurately measured in at least one dimension (longest diameter to be recorded) as ≥ 2.0 cm by chest x-ray, by ≥ 1.0 cm with CT or MRI scans, or ≥ 1.0 cm with calipers by clinical exam. All tumor measurements must be recorded in decimal fractions of centimeters.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

- 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 0.5 cm be used. If CT scans have slice thickness greater than 0.5 cm, the minimum size for a measurable lesion should be twice the slice thickness.
- Malignant lymph nodes are to be considered pathologically enlarged and measurable if it measures ≥ 1.5 cm in SHORT AXIS (greatest diameter perpendicular to the long axis of the lymph node) when assessed by scan (CT scan slice recommended being no greater than 0.5 cm).
- **Non-measurable disease**

All other lesions (or sites of disease), including small lesions (longest diameter <1.0 cm or pathologic lymph nodes with ≥ 1.0 cm to <1.5 cm short axis), are considered non-measurable disease. Bone lesions, leptomeningeal disease, ascites, pleural/pericardial effusions, lymphangitis cutis/pulmonitis, inflammatory breast disease, and abdominal masses (not followed by CT or MRI), are considered as non-measurable as are previously radiated lesions that have not progressed.

Notes on measurability:

1. For CT and MRIs, the same type of scanner should be used and the image acquisition protocol should be followed as closely as possible to prior scans. It is no longer necessary to distinguish between spiral and conventional CT.
2. Body scans should be performed with breath-hold scanning techniques, if possible.
3. PET-CT: At present, the low dose or attenuation correction CT portion of a PET-CT is not always of optimal diagnostic CT quality for use with RECIST measurements. However, if the site can document that the CT performed as part of a PET-CT is of identical diagnostic quality to a diagnostic CT, then the CT portion of the PET-CT can be used for RECIST measurements and can be used interchangeably with stand-alone CT. *The slice thickness of 0.5 cm or less is highly recommended.* If CT scans have slice thickness > 0.5 cm, the minimum size for a measurable lesion should be twice the slice thickness.
4. Ultrasound: Ultrasound is not useful in assessment of lesion size and should not be used as a method of measurement.
5. Cystic lesions that meet the criteria for radiographically defined simple cysts should not be considered as malignant lesions (neither measurable nor non-measurable) since they are, by definition, simple cysts.
6. If a target lesion becomes very small some radiologists indicate that it is too small to measure. If the lesion is actually still present, a default measurement of 0.5 cm should be applied. If the radiologist believes the lesion has gone, a default measurement of 0.0 cm should be recorded.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

10.2 Objective status at each disease evaluation

Objective Status is to be recorded at each evaluation. All measurable lesions up to a maximum of 2 lesions per organ, 5 lesions in total, representative of all involved organs, should be identified as target lesions at baseline. All other lesions (or sites of disease) including any measurable lesions over and above the 5 target lesions should be identified as non-target lesions. Measurements must be provided for target measurable lesions, while presence or absence must be noted for non-target measurable and non-measurable disease.

For studies that use disease progression as an endpoint, all potential sites of metastases should be evaluated at each time point rather than following only sites of disease identified at baseline. It is acceptable to image only the areas of the body most likely to be involved with metastatic disease for the tumor type (chest, abdomen, pelvis, and/or bone scan are typical), with the addition of any areas with suspected involvement based upon clinical symptoms. For study-specific imaging requirements, see the Study Calendar in Section 9.

- **Complete Response (CR):** Complete disappearance of all target and non-target lesions (with the exception of lymph nodes mentioned below). No new lesions. No disease related symptoms. Any lymph nodes (whether target or non-target) must have reduction in short axis to < 1.0 cm. All disease must be assessed using the same technique as baseline.
- **Partial Response (PR):** Applies only to patients with at least one measurable lesion. Greater than or equal to 30% decrease under baseline of the sum of appropriate diameters of all target measurable lesions. No unequivocal progression of non-measurable disease. No new lesions. All target measurable lesions must be assessed using the same techniques as baseline.
- **Stable:** Does not qualify for CR, PR, Progression or Symptomatic Deterioration. All target measurable lesions must be assessed using the same techniques as baseline.
- **Progression:** One or more of the following must occur: 20% increase in the sum of appropriate diameters of target measurable lesions over smallest sum observed (over baseline if no decrease during therapy) using the same techniques as baseline, as well as an absolute increase of at least 0.5 cm. Unequivocal progression of non-measurable disease in the opinion of the treating physician (an explanation must be provided). Appearance of any new lesion/site. Death due to disease without prior documentation of progression and without symptomatic deterioration (see 10.2e).

Notes on progression and new lesions:

1. For equivocal findings of progression (e.g. very small and uncertain new lesions; cystic changes or necrosis in existing lesions), treatment may continue until the next scheduled assessment. If at the next scheduled assessment, progression is confirmed, the date of progression should be the earlier date when progression was suspected.
2. FDG-PET imaging can complement regular scans in identifying new lesions according to the following algorithm.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

- Negative FDG-PET at baseline, with a positive FDG-PET at follow-up is a sign of progression based on a new lesion.
 - No FDG-PET at baseline and a positive FDG-PET at follow-up corresponding to a potential new site of disease must have a confirmation by anatomical assessment (e.g. CT, MRI, x-ray) as new site of disease to be considered progressive disease. In such a case, the date of progressive disease will be the date of the initial abnormal FDG-PET.
- 3. A previous abnormal target lymph node that became normal and subsequently enlarged in size meeting the criteria for a pathologic and measurable lymph node (a short axis of ≥ 1.5 cm) should be added to the sum of diameters to determine if criteria for progression are met based on target lesions.
- 4. A previously abnormal non-target lymph node that became normal and subsequently recurred must meet the criteria for progression based on non-target lesions to be considered progression.
- 5. A normal lymph node at baseline (<1.0 cm) that subsequently becomes pathologic is considered a new lesion and should be considered progression.
- 6. 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 becomes clear that the new lymph node has not resolved, or has increased in size, the date of progression would be the date the new lymph node was first documented.
- **Symptomatic deterioration:** Global deterioration of health status requiring discontinuation of treatment without objective evidence of progression. Efforts should be made to obtain objective evidence of progression after discontinuation.
- **Assessment inadequate, objective status unknown.** Progression or symptomatic deterioration has not been documented, and one or more target measurable lesions have not been assessed or inconsistent assessment methods were used.

Objective status notes:

1. Non-measurable and non-target measurable disease do not affect Objective Status in determination of CR (must be absent--a patient who otherwise has a CR, but who has non-measurable or non-target measurable disease present or not assessed, will be classified as having a PR). However, non-measurable and non-target lesions are included in determination of progression (if new sites of disease develop or if unequivocal progression occurs in the opinion of the treating physician).
2. An objective status of PR or stable cannot follow one of CR. Stable can follow PR only in the rare case that tumor increases too little to qualify as progression, but enough that a previously documented 30% decrease no longer holds.
3. In cases for which initial flare reaction is possible (hypercalcemia, increased bone pain, erythema of skin lesions), objective status is not progression unless either symptoms persist beyond 4 weeks or there is additional evidence of progression.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

4. Lesions that appear to increase in size due to presence of necrotic tissue will not be considered to have progressed.
5. For bone disease documented on bone scan only, increased uptake does not constitute unequivocal progression. However, increase in the soft tissue component of a lesion as measured by CT or MRI would constitute progression.
6. Appearance of new pleural effusions does not constitute unequivocal progression unless cytologically proven of neoplastic origin, since some effusions are a toxicity related to therapy or other medical conditions. Increase in the size of an existing effusion does not constitute unequivocal progression, since the fluid status of the patient could alter the size of the effusion.
7. If CR determination depends on a lesion for which the status is unclear by the required tests, it is recommended the residual lesion be investigated with biopsy or fine needle aspirate.
8. Lymph nodes are considered one organ. Only two lymph nodes should be selected as target lesions. Other involved lymph nodes should be assessed and followed as non-target lesions.
9. "Paired" organs, i.e. lungs, kidneys and ovaries, are considered one organ.
10. Pleural-based lung lesions are considered part of the lung in determining target lesions (a maximum of two lung lesions should be selected), whereas pleural effusions/thickening can be reported as a separate site.

10.3 Best Response

This is calculated from the sequence of objective statuses.

- CR: Two or more objective statuses of CR a minimum of four weeks apart documented before progression or symptomatic deterioration.
- PR: Two or more objective statuses of PR or better a minimum of four weeks apart documented before progression or symptomatic deterioration, but not qualifying as CR.
- Unconfirmed CR: One objective status of CR documented before progression or symptomatic deterioration but not qualifying as CR or PR.
- Unconfirmed PR: One objective status of PR documented before progression or symptomatic deterioration but not qualifying as CR, PR or unconfirmed CR.
- Stable/no response: At least one objective status of stable/no response documented at least 6 weeks after registration and before progression or symptomatic deterioration, but not qualifying as anything else above.
- Increasing disease: Objective status of progression within 12 weeks of registration, not qualifying as anything else above.
- Symptomatic deterioration: Objective status of symptomatic deterioration within 12 weeks of registration, not qualifying as anything else above.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

- Inadequate assessment, response unknown: Progression or symptomatic deterioration greater than 12 weeks after registration and no other response category applies.

GENERIC FOR ADJUVANT DISEASE STUDIES (RECIST 1.1)

10.0 Criteria for Evaluation and Endpoint Definitions

10.1 Progression:

Appearance of any new lesion/site. Death due to disease without prior documentation of progression and without symptomatic deterioration (see 10.2e).

Notes on progression and new lesions:

1. For equivocal findings of progression (e.g. very small and uncertain new lesions; cystic changes or necrosis in existing lesions), treatment may continue until the next scheduled assessment. If at the next scheduled assessment, progression is confirmed, the date of progression should be the earlier date when progression was suspected.
2. FDG-PET imaging can complement regular scans in identifying new lesions according to the following algorithm.
 - Negative FDG-PET at baseline, with a positive FDG-PET at follow-up is a sign of progression based on a new lesion.
 - No FDG-PET at baseline and a positive FDG-PET at follow-up corresponding to a potential new site of disease must have a confirmation by anatomical assessment (e.g. CT, MRI, x-ray) as new site of disease to be considered progressive disease. In such a case, the date of progressive disease will be the date of the initial abnormal FDG-PET.
3. A normal lymph node at baseline (<1.0 cm) that subsequently becomes pathologic is considered a new lesion and should be considered progression.
4. 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 becomes clear that the new lymph node has not resolved, or has increased in size, the date of progression would be the date the new lymph node was first documented.
5. In cases for which initial flare reaction is possible (hypercalcemia, increased bone pain, erythema of skin lesions), either symptoms persist beyond 4 weeks or there must be additional evidence of progression.
6. For bone disease documented on bone scan only, increased uptake does not constitute unequivocal progression. However, increase in the soft tissue component of a lesion as measured by CT or MRI would constitute progression.
7. Appearance of new pleural effusions does not constitute unequivocal progression unless cytologically proven of neoplastic origin, since some effusions are a toxicity related to therapy or other medical conditions. Increase in the size of an existing effusion does not

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

constitute unequivocal progression, since the fluid status of the patient could alter the size of the effusion.

10.2 Symptomatic deterioration:

Global deterioration of health status requiring discontinuation of treatment without objective evidence of progression. Efforts should be made to obtain objective evidence of progression after discontinuation.

Solid Tumor Assessment for Studies Activated since January 1, 2010 (RECIST Version 1.1)

Response Evaluation Criteria in Solid Tumors (RECIST v.1.0) was developed by the World Health Organization and mandated by the National Cancer Institute for use in SWOG solid tumor protocols on January 1, 2000. This was updated and new response evaluation criteria (RECIST v. 1.1) was released for use in SWOG protocols effective January 1, 2010.

Measurability of Lesions

Measurable disease: Measurable disease is defined differently for lymph nodes compared with other disease and will be addressed in a separate section below.

- 1) Lesions that can be accurately measured in at least one dimension (longest diameter to be recorded) as ≥ 2.0 cm by chest x-ray, by ≥ 1.0 cm with CT or MRI scans, or ≥ 1.0 cm with calipers by clinical exam. All tumor measurements must be recorded in decimal fractions of centimeters (or millimeters).

The defined measurability of lesions on CT scan is based on the assumption that CT slice thickness is 0.5 cm or less. If CT scans have slice thickness greater than 0.5 cm, the minimum size for a measurable lesion should be twice the slice thickness.

- 2) Malignant lymph nodes are to be considered pathologically enlarged and measurable if it measures ≥ 1.5 cm in SHORT AXIS (greatest diameter perpendicular to the long axis of the lymph node) when assessed by scan (CT scan slice recommended being no greater than 0.5 cm).

Non-Measurable disease: All other lesions (or sites of disease), including small lesions (longest diameter <1.0 cm or pathologic lymph nodes with ≥ 1.0 cm to <1.5 cm short axis), are considered non-measurable disease. Bone lesions, leptomeningeal disease, ascites, pleural/pericardial effusions, lymphangitis cutis/pulmonitis, inflammatory breast disease, and abdominal masses (not followed by CT or MRI), are considered as non-measurable as are previously radiated lesions that have not progressed.

SWOG
ONCOLOGY RESEARCH PROFESSIONAL (ORP) MANUAL

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

Notes on Measurability:

- 1) For CT and MRIs, the same type of scanner should be used and the image acquisition protocol should be followed as closely as possible to prior scans. Body scans should be performed with breath-hold scanning techniques, if possible.
- 2) PET-CT: At present, the low dose or attenuation correction CT portion of a PET-CT is not always of optimal diagnostic CT quality for use with RECIST measurements. However, if the site can document that the CT performed as part of a PET-CT is of identical diagnostic quality to a diagnostic CT, then the CT portion of the PET-CT can be used for RECIST measurements and can be used interchangeably with conventional CT.
- 3) Ultrasound: Ultrasound is not useful in assessment of lesion size and should not be used as a method of measurement.
- 4) Cystic lesions that meet the criteria for radiographically defined simple cysts should not be considered as malignant lesions (neither measurable nor non-measurable) since they are, by definition, simple cysts.
- 5) If a target lesion becomes very small some radiologists indicate that it is too small to measure. If the lesion is actually still present, a default measurement of 0.5 cm should be applied. If the radiologist believes the lesion has gone, a default measurement of 0.0 cm should be recorded.

Objective Status at Each Disease Evaluation:

Objective Status is to be recorded at each evaluation. All measurable lesions up to a maximum of 2 lesions per organ 5 lesions in total, representative of all involved organs, should be identified as target lesions at baseline. All other lesions (or sites of disease) including any measurable lesions over and above the 5 target lesions should be identified as non-target lesions. Note that RECIST 1.1 considers lymph nodes to be a single organ. Measurements must be provided for target measurable lesions, while presence or absence must be noted for non-target measurable and non-measurable disease.

For studies that use disease progression as an endpoint, whole body scanning at specific intervals is necessary to determine that progression is NOT present outside of the “target” areas. Therefore, in these studies it is not acceptable to image only the “target” areas of the body in follow-up scans. For study-specific imaging requirements, see the Study Calendar in Section 9.

Complete Response (CR): Complete disappearance of all target and non-target lesions (with the exception of lymph nodes mentioned below). No new lesions. No disease related symptoms. Any lymph nodes (whether target or non-target) must have reduction in short axis to < 1.0 cm. All disease must be assessed using the same technique as baseline.

Partial Response (PR): Applies only to patients with at least one measurable lesion. Greater than or equal to 30% decrease under baseline of the sum of appropriate diameters of all target measurable lesions. No unequivocal progression of non-measurable disease. No new lesions. All target measurable lesions must be assessed using the same techniques as baseline.

SWOG
ONCOLOGY RESEARCH PROFESSIONAL (ORP) MANUAL

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

Stable: Does not qualify for CR, PR, Progression or Symptomatic Deterioration. All target measurable lesions must be assessed using the same techniques as baseline.

Progression: One or more of the following must occur: 20% increase in the sum of appropriate diameters of target measurable lesions over smallest sum observed (over baseline if no decrease during therapy) using the same techniques as baseline, as well as an absolute increase of at least 0.5 cm. Unequivocal progression of non-measurable disease in the opinion of the treating physician (an explanation must be provided). Appearance of any new lesion/site. Death due to disease without prior documentation of progression and without Symptomatic Deterioration.

If a new lesion is equivocal, for example because of its small size, continued therapy and follow-up evaluation will clarify if it represents truly new disease. If repeat scans confirm there is definitely a new lesion, then progression should be declared using the date of the initial scan.

Notes regarding new lesions: FDG-PET imaging can complement regular scans in identifying new lesions according to the following algorithm.

- 1) Negative FDG-PET at baseline, with a positive FDG-PET at follow-up is a sign of progression based on a new lesion.
- 2) No FDG-PET at baseline and a positive FDG-PET at follow-up corresponding to a potential new site of disease must have a confirmation by anatomical assessment (e.g., CT, MRI, x-ray) as new site of disease to be considered progressive disease. In such a case, the date of progressive disease will be the date of the initial abnormal FDG-PET.

Symptomatic Deterioration:

Global deterioration of health status requiring discontinuation of treatment without objective evidence of progression. Efforts should be made to obtain objective evidence of progression after discontinuation.

Assessment Inadequate, Objective Status Unknown:

Progression or symptomatic deterioration has not been documented, and one or more target measurable lesions have not been assessed or inconsistent assessment methods were used.

Best Response:

This is calculated from the sequence of objective statuses. This will reflect the patient's best overall response.

- a. CR: Two or more objective statuses of CR a minimum of four weeks apart documented before progression or symptomatic deterioration.
- b. PR: Two or more objective statuses of PR or better a minimum of four weeks apart documented before progression or symptomatic deterioration, but not qualifying as CR.
- c. Unconfirmed CR: One objective status of CR documented before progression or symptomatic deterioration but not qualifying as CR or PR.

SWOG
ONCOLOGY RESEARCH PROFESSIONAL (ORP) MANUAL

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

- d. Unconfirmed PR: One objective status of PR documented before progression or symptomatic deterioration but not qualifying as CR, PR or unconfirmed CR.
- e. Stable/no response: At least one objective status of stable/no response documented at least 6 weeks after registration and before progression or symptomatic deterioration, but not qualifying as anything else above.
- f. Increasing disease: Objective status of progression within 12 weeks of registration, not qualifying as anything else above.
- g. Symptomatic deterioration: Objective status of symptomatic deterioration within 12 weeks of registration, not qualifying as anything else above.
- h. Inadequate assessment, response unknown: Progression or symptomatic deterioration greater than 12 weeks after registration and no other response category applies.

Objective Status Notes:

- 1. Non-measurable and non-target measurable disease do not affect Objective Status in determination of CR (must be absent-- a patient who otherwise has a CR, but who has non-measurable or non-target measurable disease present or not assessed, will be classified as having a PR). However, non-measurable and non-target lesions are included in determination of progression (if new sites of disease develop or if unequivocal progression occurs in the opinion of the treating physician).
- 2. An objective status of PR or stable cannot follow one of CR. Stable can follow PR only in the rare case that tumor increases too little to qualify as progression, but enough that a previously documented 30% decrease no longer holds.
- 3. In cases for which initial flare reaction is possible (hypercalcemia, increased bone pain, erythema of skin lesions), objective status is not progression unless either symptoms persist beyond 4 weeks or there is additional evidence of progression.
- 4. Lesions that appear to increase in size due to presence of necrotic tissue will not be considered to have progressed.
- 5. For bone disease documented on bone scan only, increased uptake does not constitute unequivocal progression. However, increase in the soft tissue component of a lesion as measured by CT or MRI would constitute progression.
- 6. Appearance of new pleural effusions does not constitute unequivocal progression unless cytologically proven of neoplastic origin, since some effusions are a toxicity related to therapy or other medical conditions. Increase in the size of an existing effusion does not constitute unequivocal progression, since the fluid status of the patient could alter the size of the effusion.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

7. If CR determination depends on a lesion for which the status is unclear by the required tests, it is recommended the residual lesion be investigated with biopsy or fine needle aspirate.

Baseline Disease Assessment

Typical baseline studies include: Conventional/axial or helical CT scan (with slice thickness of 0.5 cm or less), magnetic resonance imaging (MRI) scan, chest x-rays, and clinical evaluation of superficial lesions. In some cases, other studies may be included and will be outlined in Section 10.0 of the protocol.

Follow-up Studies

All repeat assessments of all disease must be done using the same method that was used at baseline in order to document the best response on treatment.

The use of differing follow-up studies after baseline may render the patient's response determination *non-assessable*. Such cases are not omitted from the study, but are reported as “non-responses” in the publication.

In some protocols, additional pathology materials from a biopsy or observation at second look surgery (done following treatment), and possibly after a second registration are required for histologic or cytologic confirmation that the patient is free of disease. These pathology materials are needed to document a pathologic assessment of tumor response including the presence or absence of disease. However, pathologic assessment does not change the clinical objective status of the patient.

Studies Utilizing iRECIST

Some studies utilize iRECIST to evaluate response or a combination of RECIST 1.1 and iRECIST for secondary endpoints. Always refer to Section 10 of the protocol to confirm and refer to the RECIST 1.1 document under Resources on the CRA Workbench that provides the key differences between RECIST 1.1 and iRECIST.

Objective Status is to be recorded at each evaluation. All measurable lesions up to a maximum of 2 lesions per organ 5 lesions in total, representative of all involved organs, should be identified as target lesions at baseline. All other lesions (or sites of disease) including any measurable lesions over and above the 5 target lesions should be identified as non-target lesions. Measurements must be provided for both target and non-target measurable lesions. Measurements must be provided for any new measurable lesions. Presence or absence must be noted for non-measurable disease.

- a. Immune-related Complete Response (iCR): Complete disappearance of all lesions (with the exception of lymph nodes mentioned below). No new lesions. No disease related symptoms. Any lymph nodes (whether target or non-target) must have reduction in short axis to < 1.0 cm. All disease must be assessed using the same technique as baseline.
- b. Immune-related Partial Response (iPR): Applies only to patients with at least one measurable lesion. Greater than or equal to 30% decrease under baseline of the

SWOG
ONCOLOGY RESEARCH PROFESSIONAL (ORP) MANUAL

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

sum of appropriate diameters of all measurable lesions. No unequivocal progression of non-measurable disease. No new lesions. All measurable lesions must be assessed using the same techniques as baseline.

- c. Immune-related Stable Disease (iSD): Does not qualify for iCR, iPR, iPD or Symptomatic Deterioration. All measurable lesions must be assessed using the same techniques as baseline.
- d. Immune-related Progression (iPD): One or more of the following must occur: 20% or greater increase in the sum of appropriate diameters of measurable lesions over smallest sum observed (over baseline if no decrease during therapy) using the same techniques as baseline; unequivocal progression of non-measurable disease in the opinion of the treating physician (an explanation must be provided); death due to disease without prior documentation of progression and without symptomatic deterioration (see Section 10.4e).
- e. Symptomatic deterioration: Global deterioration of health status requiring discontinuation of treatment without objective evidence of progression. Efforts should be made to obtain objective evidence of progression after discontinuation.
- f. Assessment inadequate, objective status unknown. Immune-related progression or symptomatic deterioration has not been documented, and one or more measurable lesions have not been assessed or inconsistent assessment methods were used.

iRECIST objective status notes:

Please note: The definitions in Section 10.4, 10.5, 10.6, and 10.7 are for **statistical consideration only**. Sites will not be responsible for monitoring these sections.

Non-measurable disease does not affect objective Status in determination of iCR (must be absent--a patient who otherwise has a iCR, but who has non-measurable disease present or not assessed, will be classified as having an iPR). However, non-measurable lesions are included in determination of iPD (if new sites of disease develop or if unequivocal progression occurs in the opinion of the treating physician).

- a. An objective status of iPR or iSD cannot follow one of iCR. iSD can follow iPR only in the rare case that tumor increases too little to qualify as iPD, but enough that a previously documented 30% decrease no longer holds.
- b. In cases for which initial flare reaction is possible (hypercalcemia, increased bone pain, erythema of skin lesions), objective status is not iPD unless either symptoms persist beyond 4 weeks or there is additional evidence of progression.
- c. Lesions that appear to increase in size due to presence of necrotic tissue will not be considered to have progressed.
- d. For bone disease documented on bone scan only, increased uptake does not constitute unequivocal iPD. However, increase in the soft tissue component of a lesion as measured by CT or MRI would constitute ir-progression.
- e. Appearance of new pleural effusions does not constitute unequivocal iPD unless cytologically proven of neoplastic origin, since some effusions are a toxicity related to therapy or other medical conditions. Increase in the size of an existing effusion does not constitute unequivocal iPD, since the fluid status of the patient could alter the size of the effusion.

RESPONSE ASSESSMENT	CHAPTER 11	REVISED: JANUARY 2025
---------------------	------------	-----------------------

- f. If iCR determination depends on a lesion for which the status is unclear by the required tests, it is recommended the residual lesion be investigated with biopsy or fine needle aspirate.

iRECIST Best Response

Please note: The definitions in Section 10.4, 10.5, 10.6, and 10.7 are for **statistical consideration only**. Sites will not be responsible for monitoring these sections.

This is calculated from the sequence of irRC objective statuses.

- a. iCR: Two or more objective statuses of CR a minimum of four weeks apart documented before iPD or symptomatic deterioration.
- b. iPR: Two or more objective statuses of PR or better a minimum of four weeks apart documented before iPD or symptomatic deterioration, but not qualifying as iCR.
- c. Unconfirmed iCR: One objective status of iCR documented before iPD or symptomatic deterioration but not qualifying as iCR or iPR.
- d. Unconfirmed iPR: One objective status of iPR documented before iPD or symptomatic deterioration but not qualifying as iCR, iPR or unconfirmed iCR.
- e. iSD: At least one objective status of iSD before iPD or symptomatic deterioration, but not qualifying as anything else above.
- f. Unconfirmed iPD: At least one objective status of iPD before symptomatic deterioration, but not qualifying as anything else above.
- g. iPD: Two or more objective statuses of iPD a minimum of four weeks apart documented before symptomatic deterioration.
- h. Symptomatic deterioration: Objective status of symptomatic deterioration within 12 weeks of registration, not qualifying as anything else above.
- i. Inadequate assessment, response unknown: iPD or symptomatic deterioration and no other response category applies.