



Disease Response

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Objectives

- Review response criteria for solid tumor cancers, lymphomas, and leukemias
 - Review how lesions are measured
 - Distinguish between responding, stable, and progressive disease
 - Demonstrate accurate and correct documentation of response
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Importance of Response

- Clinical response rates
 - Response duration or progression-free survival
 - Not all protocols assess response
 - For some protocols, response will be defined as the end point of the study
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Solid Tumor Response

- Examples of solid tumor diseases are:
 - Breast
 - Gastrointestinal (GI)
 - Genitourinary (GU)
 - *including prostate, renal, and bladder
 - Respiratory
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Key Points

- Defining RECIST
 - Defining and applying appropriate measurement methods
 - Understanding response criteria
 - Determining the patient's best overall response
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RECIST

- **RECIST: Response Evaluation Criteria In Solid Tumors**
 - Target/non-target lesions
 - Involves uni-dimensional (1-dimensional) measurements.
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Target Lesions

- Measurable lesions
 - ≥ 2 cm by regular CT or > 1 cm by spiral CT
 - maximum of 5 lesions per organ
 - 10 lesions total
 - Lesion selection
 - size and suitability for accurate repeated measurements
 - representative of all involved organs
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Non-Target Lesions

- All other sites of disease
 - Evaluable lesions
 - Lesions < 2 cm (< 1 cm by spiral CT)
 - Record as present or absent on the measurement form
 - Examples of non-target lesions: Bone, Leptomeningeal disease, (Brain/CNS), Ascites, Abdominal masses (not confirmed by imaging), Pleural/pericardial effusion, Cystic lesions, Tumors situated in previously irradiated areas
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Reporting Lesions

- Report on the measurement form
 - Must have at least one target lesion (for studies that require measurable disease)
 - Target lesions: Report lesion's longest diameter (LD) in centimeters
 - Non-target lesions: Report as "present" or "absent"
 - Sum of all LDs for baseline and subsequent assessments
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Evaluation of Lesions

- Complete Response (CR)
 - Partial Response (PR)
 - Stable Disease (SD)
 - Progressive Disease (PD)
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Complete Response

- Disappearance of all target and non-target lesions
 - Normalization of tumor marker level
 - *Example:* Prostate Specific Antigen (PSA)
 - Requires confirmation at least 4 weeks later
 - No new lesions
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Partial Response

- Recognized in target lesions only
 - $\geq 30\%$ reduction in sum of longest diameters from baseline
 - Requires confirmation at least 4 weeks later
 - No new lesions
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Stable Disease

- Target Lesions
 - Insufficient decrease in sum of the longest diameters to qualify as a Partial Response
 - Insufficient increase in sum of the longest diameters to qualify as a Progression
 - Non-Target Lesions
 - Persistence of non-target lesion(s)
 - Maintenance of tumor marker level
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Progression/Relapse

- At least a 20% increase in the sum of the longest diameters of all target lesions; compared to the *smallest* sum longest diameter since starting protocol
- OR
- Appearance of one or more new lesions (target and/or non-target)
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Tips for Tumor Measurement

- Follow all lesions measured at baseline
 - Only report longest diameter of each lesion
 - Record measurements in cm
 - Use consistent imaging methods
 - Confirm with repeat measurements
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**Lymphoma
and
Leukemia
Response**

Lymphoma Disease Types

- Non-Hodgkin Lymphoma (NHL)
 - Hodgkin's Disease (HD)
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Three Factors Impacting Disease Response

- Measurable disease
 - Most CALGB studies require patients to have measurable disease
 - Tumor mass measuring $>1\text{cm}$
 - Assessable disease
 - Bone marrow status
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Lymphoma Measurable Disease

- Select a maximum of 6 lesions with the following features:
 - Measurable in at least 2 perpendicular dimensions
 - Representative of all involved organs/areas
 - Suitable for accurate repeat measurements
 - Include mediastinal and retroperitoneal areas of disease
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Lymphoma Measurable Disease

- Report bi-dimensional nodal measurements
 - Select sites and measure two longest diameters
 - Multiply each node's two longest diameters together
 - Sum the Products of the greatest transverse Diameters (SPD) (Tumor Size)
 - Double check calculations
 - Use correct units (cm)
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Lymphoma Non-Measurable Disease

- Assessable disease
 - Masses that **cannot** be measured bi-dimensionally
 - Organ involvement (liver and spleen)
 - Recorded as
 - “present” at baseline
 - “no change”, “increased”, “decreased”, “absent” at follow-up
 - Bone marrow status
 - Positive or Negative for lymphoma cells
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Lymphoma Response Assessment Table

Measurable Sites	Assessable Sites (e.g., liver spleen)	Bone Marrow	Overall Response
CR	CR	Negative	CR
CRu	CR	Negative or Indeterminate	CRu (CR – unconfirmed)
CR	CR	Indeterminate	CRu (CR – unconfirmed)
PR	No Increase	Irrelevant	PR
CR	Decrease	Irrelevant	PR
CR	No Increase	Positive	PR
SD	No Increase	Irrelevant	SD
New or Increased	Irrelevant	Irrelevant	Relapse or PD
Irrelevant	Irrelevant	Positive (after a CR)	Relapse or PD
Irrelevant	New or Increased	Irrelevant	Relapse or PD

Standard Lymphoma Response

- Complete Response (CR)
 - Complete Response Unconfirmed (CRu)
 - Partial Response (PR)
 - Stable Disease (SD)
 - Progression/Relapse (PD)
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Complete Response (CR)

- Free of all lesions, disease-related symptoms, and biochemical abnormalities
 - Nodes and nodal masses are normal size
 - Enlarged organs have decreased in size and are free of macroscopic nodules
 - Bone marrow is clear of disease
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CR Unconfirmed (CRu)

- Free of all disease and symptoms
 - Enlarged organs have decreased in size and are free of macroscopic nodules
 - Residual nodes >1.5 cm have regressed 75%
 - Presence of residual abnormality (scarring)
 - Indeterminate bone marrow
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Partial Response (PR)

- $\geq 50\%$ decrease of the tumor size (SPD) using the 6 largest nodes or masses
 - No size increase of other nodes, liver, or spleen
 - Splenic and hepatic nodules regressed by $\geq 50\%$
 - No new sites of disease
 - Bone marrow assessment irrelevant
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Stable Disease (SD)

- Insufficient shrinkage to qualify for a Partial Response
 - Insufficient increase to qualify for a Progression
 - Refer to the smallest tumor size achieved since treatment started, which may not necessarily be the baseline measurement
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Progression/Relapse (PD)

- Increase $\geq 50\%$ in the total tumor size
 - Appearance of any new lesions
 - Positive bone marrow after achieving a Complete Response
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Three Factors Impacting Leukemia Response

- Hematologic features
 - ANC, platelet counts, hemoglobin
 - Bone marrow features
 - Cellularity and blast cell percentage
 - Clinical features
 - Lymphadenopathy/Splenomegaly/CNS involvement
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Standard Leukemia Response Types

- **Always** refer to the Criteria for Response section of the protocol for specifics.
 - Response terminology and criteria in leukemia are disease specific.
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General Response Criteria for Leukemia

- Complete Response (CR)
 - Disappearance of signs and symptoms of disease
 - Peripheral blood counts within normal limits
 - Partial Response (PR)
 - Decrease in white blood cell count or peripheral lymphocyte count
 - Reduction in size of enlarged organs
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General Response Criteria for Leukemia

- Progression/Relapse (PD)
 - Increased WBC or platelet count (CML)
 - Increase in size of liver or spleen (CML/CLL)
 - Appearance of new lymph node (CLL)
 - Finding circulating blasts cells in peripheral blood or > 5% myeloblasts in bone marrow (AML/ALL)
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Resources

- Protocol
 - www.calgb.org
 - www3.cancer.gov/dip/RECIST.htm
 - www.cancer.gov (NCI)
 - Data Coordinator at the CALGB Statistical Center in Durham, NC
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Remember:
***Best overall
response
cannot worsen
over time!***