

# Considerations in Defining Disease Recurrence in Adjuvant RCC Trials

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# Topics for Discussion

- What defines no evidence of disease on study entry?
- Do we need to biopsy all lesions when safe/feasible? If so, what date counts as recurrence: biopsy or date of radiographic recurrence?
- What counts as unequivocal radiographic recurrence on study?
- How do we deal with non-specific findings on study entry or on surveillance imaging?

Trial	Entry Criteria	PD Criteria	Basis
Trials 1 and 2	<ul style="list-style-type: none"> <li>No evidence of residual macroscopic disease on post-operative CT scan.</li> <li>Patients with a pulmonary nodule may be eligible but only if the nodule is &lt;5mm diameter and stable for at least 3 months by CT</li> </ul>	<ul style="list-style-type: none"> <li>If a patient should experience clinical signs of progressive disease (PD) at any point, this should be confirmed via CT/X-ray or a positive biopsy.</li> <li>No specified criteria otherwise (investigator's discretion)</li> </ul>	<ul style="list-style-type: none"> <li>Clinical consensus of Investigators</li> </ul>
Trials 3 and 4	<ul style="list-style-type: none"> <li>Patients must have no clinical or radiological evidence of distant metastases, i.e., patients must be M0.</li> </ul>	<p>Any recurrence of malignant disease should be proven by core needle biopsy whenever possible</p> <ul style="list-style-type: none"> <li>Positive cytology or biopsy</li> <li>If biopsy is not possible of a solitary new lung, soft tissue, or visceral lesion that is <math>\geq 1</math> cm, confirmation of growth by at least 5mm or appearance of other new lesions on subsequent scans at least 4 weeks later.</li> <li>If biopsy is not possible of a lymph nodes <math>\geq 1.5</math>cm in short axis, confirmation of growth by at least 5mm or appearance of other new lesions on subsequent scans at least 4 weeks later.</li> <li>For bone lesions: A positive radiographic study such as bone scan with 2 or more new lesions that are confirmed with MRI or CT. For a solitary lesion or equivocal finding on a scan, biopsy is required or subsequent scans demonstrating growth or at least one new lesion at least 4 weeks later.</li> <li>For brain lesion(s), a positive brain CT or MRI is acceptable without a biopsy or confirmation.</li> </ul>	<p>Cooperative Group Trials: based on other disease templates and what regulatory bodies had approved in past, discussion with FDA and what would have constituted measurable disease by RECIST (when applicable) if not amenable to biopsy</p>

Trial	Entry Criteria	PD Criteria	Basis
Trials 3 and 4	<ul style="list-style-type: none"> <li>• No metastatic disease by independent review</li> <li>• ANY radiographic abnormality = mets</li> </ul>	<ul style="list-style-type: none"> <li>• Biopsy whenever possible</li> <li>• Multiple small (<math>\leq 1</math> cm) lung lesions or a single lung lesion <math>&gt; 1</math> cm</li> <li>• Enlarging lesions in the renal bed, LNs, liver and soft tissues were required to be <math>\geq 1.5</math> cm, long axis</li> <li>• Brain lesion(s)</li> <li>• Multiple areas of bone uptake, solitary bone lesions required additional imaging</li> <li>• Pleural effusion with an associated soft tissue mass/enhancing rim or ascites</li> </ul>	

What Defines No Evidence of Disease on  
Study Entry?

# Considerations for Radiologic Entry Criteria on Adjuvant RCC Trials

- Time from surgery to scan
- No evidence of macroscopic disease on postoperative CT scan
- Pulmonary nodules acceptable with certain criteria? Follow up ?
- Enlarged lymph nodes acceptable with certain criteria? Follow up ?

# Considerations for Radiographic Disease Recurrence

# Considerations for Defining Lung /Soft Tissue Recurrence in Adjuvant RCC Trials

Biopsy where feasible for solitary new lung/soft tissue lesions, what size ? False negative?

Where biopsy is not feasible, considerations for confirmation of growth on subsequent scans or appearance of new lesions to confirm recurrence

Number of smaller lung nodules ?



# Considerations for Defining Lymph Node Recurrence in Adjuvant RCC Trials

- Biopsy where possible, what size? False negative?
- Lymph nodes  $\geq 1.5\text{cm}$  short axis
- Confirmation of growth by at least 5mm ? or appearance of new lesions on subsequent scans
- Time to subsequent scans
- Define timepoint of recurrence

# Considerations for Defining Bone Recurrence on Adjuvant RCC Trials

Positive bone scan with 2 or more lesions confirmed on CT or MRI. What about 1 ?

For solitary lesions, subsequent scan to demonstrate growth or at least one new lesion at least 4 weeks apart

Biopsy?

# Considerations for Disease Recurrence in Adjuvant RCC Trials

Site of disease recurrence	Considerations for Discussion
Pleural effusion	Cytology positive for malignancy or associated with a mass
Brain/CNS	Brain lesions on CT or MRI
Liver	Abdominal CT or MRI demonstrating lesion that is $\geq 1$ cm with confirmation of growth by at least 5 mm or appearance of one or more new lesions $\geq 1$ cm on subsequent scans at least 4 weeks later
Soft Tissue Mass	Enlarging solid masses as evidenced by 2 CT or MRI imaging studies separated by at least 4 weeks  Any soft tissue mass $\geq 1$ cm?

# Indeterminate Lesions and Lesions Not Amenable to Biopsy

- Classifying abnormal imaging findings
  - Unequivocal recurrence
  - Highly suspicious lesions
  - Indeterminate lesions
- Specifying common processes to evaluate abnormal findings
- Defining appropriate radiographic follow up