# RECIST 1.1 questions and clarifications:

## The definition of SD:

Issue:
In the main article on page 233 the definition of SD is written as; "Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study." It should read;

Answer:

"Neither sufficient shrinkage (compared to baseline) to qualify for PR nor sufficient increase (taking as reference the smallest sum diameters while on study) to qualify for PD

## Lesions less than 5 mm

Issue:
In the main paper it suggests lesions that reduce in size to less than 5 mm should be measured if possible. However it also says that if a lesion is present but not measurable it should be assigned a nominal value of 5 mm.

Answer:
Adhere to the rule, if it is measurable, then record the measurement. If you cannot measure, then record it as 5 mm.

## Abnormal lymph node

Issue:
If an abnormal lymph node (recorded as Target or Non Target) 'disappears' (i.e cannot be seen for Non Target nodes or is < 10 mm) but then 'reappears' (I.e. visible for Non Target nodes or ≥ 10mm for nodes considered Target lesions at baseline) is this considered to be continued CR or PD?

Answer:
Lesions that disappear and reappear do not automatically = PD unless

- Other criteria are also met (new lesions, ↑ Sum of Measure (SOM) ≥ 20%) OR
- CR (overall) was definitively (*) assigned at the previous assessment. In this scenario, the reappearance of any malignant non nodal lesion = PD.
  - Nodes require special consideration as nodes <10 mm are considered benign. Thus, if a node is only considered to have 'reappeared' if it is ≥ 10 mm (Target lesion) or has unequivocally progressed (Non Target lesion).
  - As always, the overall context must be considered. Patients with bulky non nodal disease in CR, in whom a single node becomes visible on a CT scan, with no evidence of recurrence elsewhere should ideally be reimaged prior to a decision regarding recurrence being made.

*(*) It is recommended that CR previous cycle be confirmed – lesions may have in fact always been present but have been indistinct. In such cases, PR may be the appropriate for both assessments*

## Two target lesions

Issue:
How should 2 target lesions per organ be applied to lymph nodes. Can individual chains/regions be considered 1 organ or is lymph nodes (all locations included) a single organ?

Answer:
Nodes are considered to be one organ. If there are multiple chains/regions, consider selecting one from each. For hematologic malignancies, modified criteria could be considered.

## Double the slice thickness/interval & lymph nodes

Issue:
Should double the slice thickness/interval be applied to lymph nodes as well? In other words, if slice thickness is 10 mm, should measurable lymph nodes be 20 mm in short axis or are 15 mm nodes still considered measurable?

Answer:
It is strongly recommended that slice thickness of 5 mm should be used.

## FDG-PET correlation with CT

Issue:
The section on FDG-PET mentions that correlation with CT is warranted for new lesions, and that PD should be declared if the hot spot on PET corresponds to a progressing lesion on CT. How should this correlation be made if the hot spot on PET corresponds to a target lesion that has enlarged but the SOM does not show an increase that is sufficient for PD (other target lesions has not enlarged or have actually decreased). Is this PD?

Answer:
No. FDG-PET is complementary but does not override measurement rles of RECISTS 1.1 rules for 20% being progression.

## FDG-PET hot spot not associated with a new CT (or MRI) lesion

Issue:
If there is a hot spot on FDG-PET (baseline PET was not available) that is not associated with a new CT (or MRI) lesion, the article states that PD should not be declared. What should response be, NE?

Answer:
No. The patient has been assessed with CT or MRI, and thus the response should be assigned based on that imaging.

## Text in relation to content table 1

Issue:
The text does not seem to fully support the content of table 1 in page 235 of the article, with

regards to non-target lesions being NE. Can you please confirm the overall responses in the following scenarios?
According to the article, a reappearing lesion is not PD if the prior patient 'status' was PR or SD. Does 'prior patient status' refer to the target lesion assessment or the overall response? In case there is only 1 target lesion and it disappears, then target lesion assessment is CR, however, non-targets are non-CR/non-PD and therefore, overall response is PR. What should the nadir be for assessment of the only target lesion if it reappears?

Answer:
Prior status refers to the overall response, not each lesion alone. Only with an overall response of CR would the 'reappearance' of malignant target or non- target lesions be considered PD.
In the example given of only one target lesion, with no non target lesions, if the target lesion disappears and then re-appears, this would be considered to be PD, providing that if the lesion is a node, it was ≥ 10 mm (i.e malignant). However, a single target lesion that disappears and reappears, with stable non target lesions, would not be considered PD.